



Ethical Principles in european regulation of biotechnology - possibilities and pitfalls

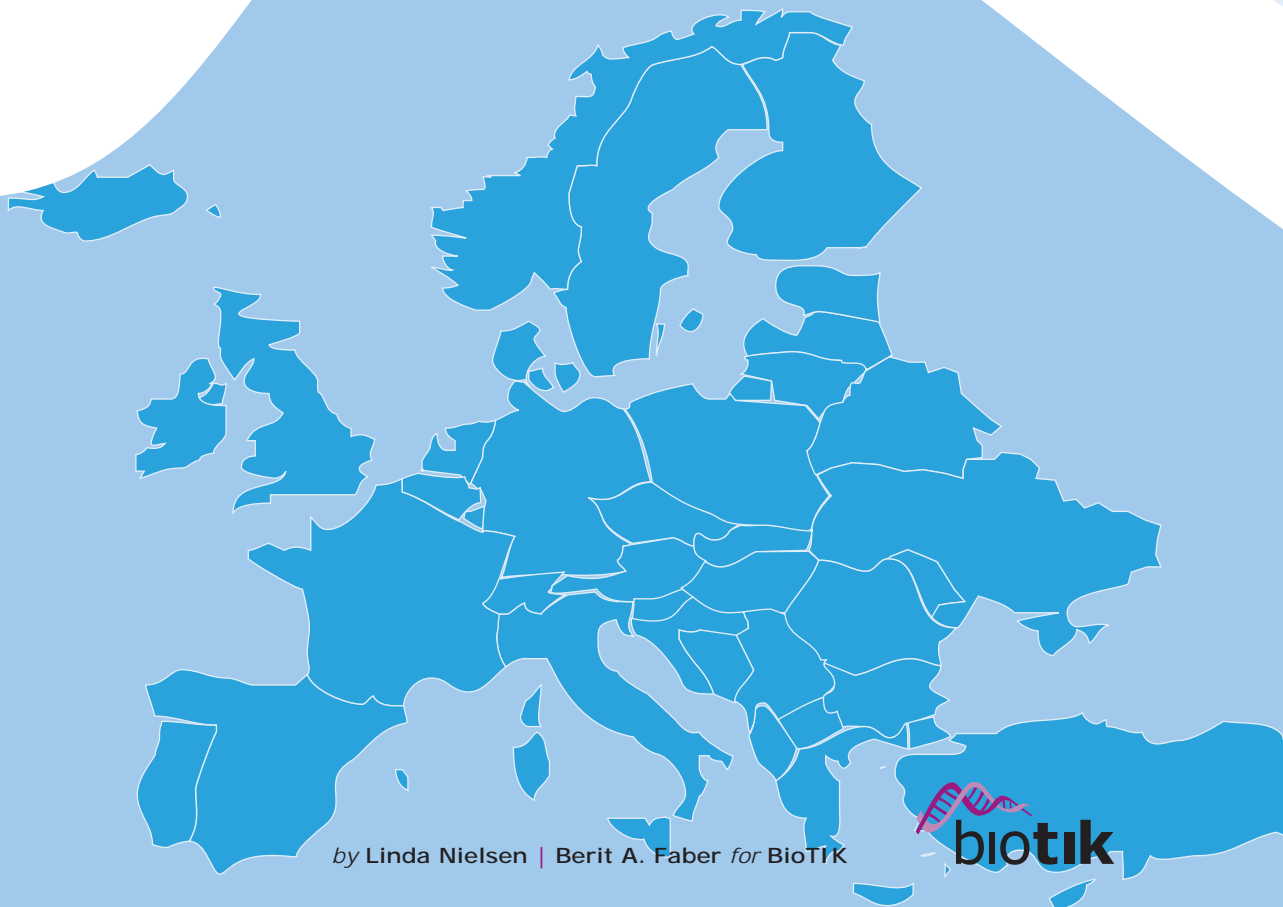
Nielsen, Linda ; Faber, Berit A.

Publication date:
2002

Citation for published version (APA):
Nielsen, L., & Faber, B. A. (2002). *Ethical Principles in european regulation of biotechnology - possibilities and pitfalls*. Ministry of Economic and Business Affairs, Denmark.

Ethical principles in european regulation of biotechnology

- possibilities and pitfalls



by Linda Nielsen | Berit A. Faber for BioTik

COPENHAGEN 2002

biotik



About BioTIK

In 2001 the Danish Parliament launched the BioTIK-project. It is a four-year project focusing on both the possibilities that gene technology offers, and the ethical principles that are to be considered in order to make the right decisions. BioTIK is a Danish abbreviation of biotechnology and ethics.

Hence nine Danish Ministries have joined a Task Force with the purpose to incorporate ethical principles in regulation of biotechnology, in decision making processes and as a basis for public perception and information. Read more about the BioTIK-project at www.biotik.dk.

Ethical principles in European regulation of biotechnology - possibilities and pitfalls by Linda Nielsen and Berit A. Faber:

ISBN 87 7408 663 4

The Ministry of Economic and Business Affairs,
Denmark 2002

National Consumer Agency, BioTIK-Secretariat,
Amagerfaelledvej 56, DK 2300 Copenhagen.

Telephone + 45 32 66 90 00

Fax + 45 32 66 91 00

E-mail: biotik@biotik.dk

Impression: 1000

The report is also available on the Internet at:
www.biotik.dk

Translation: Scandinavian Translators A/S

Layout and printing: aparte as

Foreword

The present report was prepared by Professor Linda Nielsen, PhD, and Berit A. Faber, Head of Secretariat, L.L.M, in collaboration with the BioTIK Secretariat, the National Consumer Agency of Denmark. During the preliminary research and final preparation of the report, Gisela Hildebrandt and Troels Koch, students of law, provided skilled and dedicated assistance with Internet searching and typing up of the final document.

The purpose of the report is to describe, analyse and assess the varying methods of operationalising ethical principles within European regulation of biotechnology, with the inclusion of proposals for different tools and models for use in future regulation. The aim of the report is first and foremost to serve as a practical resource for use in evolving regulation, political support, and democratic and debating activities in different domains in response to rapid advances in biotechnology, and the ethical concerns that follow in its wake. Accordingly, we have chosen to provide only a limited number of notes to document sources. The individual statements are expanded on in the report's appendices, where further documentation is provided. We hope that the report will contribute to supporting the aim of developing the life sciences and biotechnology in accordance with ethical values and societal aims, in line with the description in the EU Commission's strategy on "Life Sciences and Biotechnology - A Strategy for Europe", as now ratified by the EU's Council of Ministers. The EU Commission's strategy for life sciences and biotechnology testifies to the fact that deliberations on operationalisation of the ethical principles which biotechnology raises are currently ongoing in many countries and at many levels, and it is our hope that this report with its "toolbox", "buffet" and "menu" may serve to consolidate and inspire these deliberations.

Contents

PART ONE: Introduction and general issues

1 INTRODUCTION	10
1.1 Background	10
1.2 Purpose	10
1.3 Methods	11
2 ETHICS AND ACTORS	12
2.1 Fundamental ethical principles	12
2.1.1 Economic and qualitative benefits	12
2.1.2 Autonomy, dignity, integrity and vulnerability	12
2.1.3 Just distribution of benefits and burdens	12
2.1.4 Co-determination and openness	12
2.1.5 General deliberations on the regulation of ethical issues	12
2.2 Different actors	13
2.2.1 Researchers, commercial actors and other affected parties	13
2.2.2 Decision-makers and administrators	14
2.2.3 The media and the general public/lay people	14
3 RISK ASSESSMENT - BETWEEN SCIENCE AND VALUES	15
3.1 Beyond the objective risk concept	15
3.2 Biotechnology as a risk narrative	16
3.3 The communication of risk as a dialogue about uncertainty	18

PART TWO: Regulation of biotechnology at international and national level

4 REGULATION - OVERVIEW	22
4.1 International regulation	22
4.2 The Council of Europe	23
4.3 The EU:	23
4.3.1 The authorisation system for medicinal products	23
4.3.2 EU authorisation system for GMOs, plants and foods	24
4.3.3 Other EU regulation, etc.	25
4.4 National regulation in the field of health	26
4.5 The international picture and differences in the intensity of national regulatory activity	27

5 ANALYSIS OF THE REGULATORY PICTURE	29
5.1 "Ethics where?" - coverage and scope of ethical principles	29
5.2 Medicinal products, plants and foods - ethics	30
5.3 The "ethics of how?" - different models for operationalisation	30
5.3.1 Broad, discretionary or precise provisions	30
5.3.2 Regulation of content versus process	33
5.4 Incorporation of the four ethical principles	33
5.5 Summarising analysis - "gaps in Community regulation"	34

PART THREE: Tools for incorporating ethical principles

6 DEMOCRATISATION TOOLS AND DEBATE MODELS	38
6.1 Ethical councils (debate and advice)	38
6.1.1 Nomination and members	38
6.1.2 Objective	39
6.2 Scientific ethics committees (authorisations)	39
6.2.1 The committees' composition	39
6.2.2 Areas of responsibility	40
6.2.3 Assessment criteria	40
6.3 Other democratisation tools	41
6.3.1 Technology councils, including consensus conferences	41
6.3.2 Future panel	41
6.3.3 Values workshop - Norway	41
6.4 Cooperation between councils and boards	42
6.5 Analysis and evaluation of democratisation instruments	43
6.5.1 Representation of experts and of lay people	43
6.5.2 The purpose and role of the committees	45
6.5.3 Criteria for ethical evaluation	46
7 REGULATORY INSTRUMENTS	47
7.1 Regulatory function	47
7.1.1 The normative function	47
7.1.2 The protective function	47
7.1.3 The technical function	47
7.2 Different types of regulatory instruments	48
7.3 Advantages and drawbacks of different regulatory models	49

8 THE TOOLBOX - CHECK-LIST	52
8.1 Regulatory models	52
8.1.1 Choice of forum	52
8.1.2 Choice of type	52
8.2 Debate models	53
8.2.1 Consensus conferences etc.	53
PART FOUR: Ethical principles in European regulation	
9 CONCLUSIONS AND RECOMMENDATIONS	56
9.1 Introduction	56
9.2 Can experience from the human area be applied to the foods area?	56
9.3 Ethical principles in the foods area?	59
9.4 How are ethical principles operationalised in regulations?	60
9.4.1 Regulatory challenges and possible tools	60
9.4.2 Political will and regulatory scope	61
9.4.3 Actors: role and scope of action	62
9.4.4 Debate: polycentrism and timing	65
9.5 A choice of tools	65
9.5.1 The debate models	65
9.5.2 National regulation	66
9.5.3 International regulation	66
9.6 Conclusion	67
10 PROSPECTS AND CHALLENGES	70
11 POSTSCRIPT	71

PART ONE

INTRODUCTION GENERAL ISSUES

- Ethical principles
- Different actors
- Risk assessment -
between science and values

1 Introduction

Biotechnology, bioethics and biolaw are important issues on the agenda both nationally and internationally - and not least with regard to the EU. One of the reasons for this is the transcendental nature of biotechnology as concerns national borders, impacts and cultures. It offers hope of major breakthroughs in a wide range of areas, but, equally, gives rise to concerns about the negative impacts and breaches of fundamental ethical values that it may entail. A series of questions therefore arise about how the positive aspects of biotechnology may be put to use and supported while, at the same time, avoiding potentially undesirable aspects and impacts. In this sense, ethical principles in Community regulation of biotechnology are a central issue.

Bioethics can help to provide pointers as to which applications and impacts are to be considered either desirable or undesirable. Regulation can then help to impose limits on the application of biotechnology on the basis of these ethical principles, and to ensure that the governance and control of such application take place in accordance with democratic values, such as dialogue, participation and equity. In this way, regulation reflects ethics, while also serving to guide ethical evaluation.

1.1 Background

The new biotechnologies, involving genetic engineering and cloning as well as genetically modified organisms (GMOs), raise a large number of new and difficult questions about how these technologies are to be tackled - from a political, ethical and legal perspective. We are faced with a melting pot in which ethical questions and the prospects for governance of human health, food and the environment, as well as the rights of different individuals and groups intermingle and become interdependent. The ethical principles have to be weighed against each other and operationalised in regulation. This process is exceptionally difficult, but is increasingly necessary in a growing number of areas.

The EU has a central role in the process, both by virtue of its directives and its ethics committees and debates in the European Parliament. Matters of special importance include the EU's role vis-à-vis the moratorium on GM products, the precautionary principle, the Charter of Fundamental Rights and regulation of the marketing of foods and medicinal products. At the

same time, in recent years, regulation has been introduced in a large number of EU member states, which, with varying aims and intensity and employing different means, has sought to strike a balance between promoting and controlling biotechnology.

1.2 Purpose

The purpose of this report is to describe, analyse and assess the varying methods of operationalising ethical principles within European regulation of biotechnology, with the inclusion of proposals for different tools and models for use in future regulation.

Part One describes the issues, and presents the ethical principles involved. The fundamental dilemmas inherent in operationalising ethical principles in regulation in one way or another are also introduced; similarly, the actors present in the area and the way in which risk assessment is situated between science and values are also covered.

Part Two outlines regulation in the field of biotechnology in the EU. The aim here is not to offer an exhaustive description of the particulars of regulation, but to offer an at-a-glance view, which, it is hoped, will facilitate deliberations on regulatory models from a broader perspective. The outline covers general international regulation, including regulation ratified by the European Union, as well as a kaleidoscopic picture of national regulation in the individual EU member states. Additionally, we provide a brief walk-through of regulation in the different fields of biotechnology, since regulation varies considerably according to the issue it covers, e.g. medically assisted procreation or foods, etc. Attention will be drawn to the principal common denominators and differences.

Part Three describes a range of tools for operationalising ethical principles, and the advantages and drawbacks of individual tools are described and assessed. The report covers tools for democratising the decision-making process ("debate models"), traditional regulatory instruments (legal acts, administrative directives and the like), as well as other instruments, including case law, professional standards and education. We then go on to provide a "check-list" for a number of the decisions that need to be made with respect to choice of forum, form and content of regulation and/or the democratic process whereby the ethical principles are to be operationalised. The various options are presented metaphorically in the

form of a "buffet" of different "dishes" for composing a complete "meal".

Part Four focuses on how the "toolbox" can be employed constructively. In this context we will be considering how lessons learned in the "human health area" e.g. the treatment of patients and scientific ethical evaluations, might be incorporated in the foods area. Drawing on the analysis of the advantages and drawbacks of the various tools, a series of different proposals for solutions will be indicated. In recognition of the fact that different countries have different backgrounds and traditions as regards culture, religion, structures, regulatory traditions and so on, the aim is not to dictate the "correct" use of the toolbox, but to propose a range of options. In other words, we return to the idea of a "menu" from which alternative "meals" may be assembled.

For the Danish version of the report, an appendix section is provided, which includes a more detailed report on legislation in the area, a list of links and an overview of selected ethical provisions from the EU regulation of medicinal products and foods. The last of these appendices is in English.

1.3 Methods

Relevant, up-to-date legislation on selected biotechnology areas for selected countries has been collated. Since this regulation is evolving rapidly and is subject to frequent amendment, a detailed description of legislation in the individual countries has not been attempted, but instead a panoramic view, as a means of obtaining a general perspective. As a dynamic, practicable aid to finding the relevant regulation, etc. Appendix 1 contains a collection of links to the appropriate websites.

The selected areas comprise legislation of medically assisted procreation, genetic testing and gene therapy, biobanks, medical research and clinical trials involving humans, cloning, genetically modified animals, xenotransplantation and genetically modified foods. The countries selected for detailed study are the UK, France, Germany, Sweden, The Netherlands, Denmark and Norway (even though Norway is outside the EU).

The report is to a large degree based on our experience as legal experts, which includes participation over many years in legislative work within the Danish framework, collaboration on bioethics and regulation at the Nordic

level, and legal work under the auspices of the EU and in relation to the Council of Europe. At the same time, we have worked for many years with ethical issues, both as President/Head of Secretariat of the Danish Council of Ethics and in relation to the EU (as a member of EGE) and the Council of Europe (participation in the consultations on the Convention on Human Rights and Biomedicine). Finally, we have attended a large number of conferences, seminars, etc. on biolaw and bioethics at the international level.

The deliberations on the advantages and drawbacks, experiences, etc. of different tools are based partly on our own experiences, and partly on a series of discussions over the years with a range of people familiar with the area. It follows that no attempt is made to present scientific truths, but rather a number of opinions, which may often be subjective, and which may be expressed differently outside the country that originally produced a given instrument. Nonetheless, we have felt it appropriate to include these reflections, since, it is hoped, they may aid the process of selecting tools and menus.

The aim of the report is first and foremost to serve as a practical resource for use in evolving regulation, political support, and democratic and debating activities in different domains in response to rapid advances in biotechnology, and the ethical concerns that follow in its wake. Accordingly, we have chosen to provide only a limited number of notes to document sources, etc. The individual statements are expanded on in the report's appendices, where further documentation is provided.

We hope that the report will contribute to supporting the aim of developing the life sciences and biotechnology in accordance with ethical values and societal aims, in line with the description in the EU Commission's strategy on "Life Sciences and Biotechnology - A Strategy for Europe", as now ratified by the EU's Council of Ministers.

The EU Commission's strategy for life sciences and biotechnology testifies to the fact that deliberations on operationalisation of the ethical principles which biotechnology raises are currently ongoing in many countries and at many levels, and it is our hope that this report with its "toolbox", "buffet" and "menu" may serve to consolidate and inspire these deliberations.

2 Ethics and actors

2.1 Fundamental ethical principles

There can be little doubt that biotechnology heralds substantial prospects for the positive development of both national and international society, yet our ability to unlock these potentials is conditional on our response to a number of key ethical issues. One of the most fundamental aspects is the need to incorporate the ethical principles borne out of concerns about how biotechnology might impact on values and rights in a way that is considered undesirable. Biotechnology confronts us with a range of ethical and political challenges by putting the focus on fundamental human values. Once the individual person, profession, clinic, or country, or the European Union, etc. assumes a stance on how biotechnology is to be utilised, ethical evaluations become essential.

Since the focus in this report is devoted especially to "tools" for incorporating ethical principles, no thoroughgoing description and analysis is made of the diversity of ethical viewpoints and positions that exist within the scientific debate on this question.¹ This should also be seen in the light of the fact that, within national boundaries, there will be internal debates on how ethics are to be defined and implemented in detail, just as at the international level there is a difference in which ethical schools and movements are most prominent. It is, however, necessary to specify which elements these ethical principles contain in each case. This is a question of a choice, which is open to discussion, but which nonetheless is judged to include the most important elements to have gained a foothold in current ethical science and literature. The ethical signposts employed in the following can be divided into four "sets":²

2.1.1 Economic and qualitative benefits

Biotechnology is to be employed for the benefit of human beings, society and nature. There is, therefore, an assumption that, for any potential risk to be acceptable, the technology should not simply serve financial interests, but also contribute to an improved quality of life, e.g. in the shape of better foods, an improved environment or better health.

2.1.2 Autonomy, dignity, integrity and vulnerability

In the application of biotechnology, regard must be shown for human autonomy and dignity and for the integrity and vulnerability of human beings, animals and the natural world.

2.1.3 Just distribution of benefits and burdens

Biotechnology should be employed in such a way that it does not impede our efforts to create a society in which benefits and burdens are fairly distributed. This consideration applies both within the individual society and in relation to the creation of growth which is sustainable when seen in relation to other countries, including developing countries, and in relation to future generations.

2.1.4 Co-determination and openness

Decisions to use or not to employ genetic engineering should be made through an open process, where respect is given to all viewpoints.

These four fundamental principles should be understood as parameters to be made substantive and operationalised through democratic debate. Decisions on the utilisation of biotechnology will often be the result of a series of complicated balances, and these balances may differ within different aspects of life, from country to country, and within different professions and cultures.

2.1.5 General deliberations on the regulation of ethical issues

Ethical issues may be embodied in legislative regulation in two basic ways. Firstly, ethical considerations can lead to standardisation of content, such that the administrative authorities can instantly determine, on the basis of ethical rules in the legislation, whether something is prohibited or is permissible. An example of this would be the prohibition of cloning. Secondly, ethical issues may be embodied in standardisation of procedure, such that the administrative authorities need to make a ruling on whether something is prohibited or can be permitted, after a closer examination of the case, which will also involve assessments and decision-making about ethical aspects. An example of this would be the EU directive on good clinical practice (GCP directive).

¹ For discussion of this question, see (inter al.) Jacob Dahl Rendtorff and Peter Kemp: "Basic ethical principles in European bioethics and biolaw. Report to the European Commission, 2000", Peter Kemp, Jacob Rendtorff and Niels Mattsson Johansen (eds.): "Bioethics and biolaw", Rhodos International Science and Art Publishers and Central for ethics and law, Copenhagen 2000.

² The categorisation was originally produced for a report from the then Danish Ministry of Economic and Business Affairs: "Regeringens redegørelse til Folketinget om Etik og Genteknologi" [The Danish Government's Report on Ethics and Genetic Engineering as presented to the Danish Parliament] from 2001.

International regulation will typically contain obligations in relation to the content of national legislation, but which permit a certain discretion as to the implementation of, for example, an international convention in national legislation. International regulation, however, does not normally impose direct obligations on national authorities.

EU regulation does place demands upon national regulation (directives), but can also have an immediate direct effect in relation to citizens and businesses (regulations).

Finally, EU regulation may impose requirements on EU courts or EU decision-making processes in so far as the decision-making competence is not purely national. EU regulation of biotechnology is content-based in relation to citizens and businesses, as well as procedure-based, and, for the latter, it involves both decision-making processes related to EU courts and national decision-making processes.

National regulation applies directly to the individual citizen or business, and can contain standardisation of both content and procedure.

Ethical criteria do not come with a handy book of answers in which we can look up whether a method of treatment or a GMO-based crop is permissible or not. But we can point to some ethical considerations, which should form part of any overall assessment prior to a ruling on whether a method of treatment or a crop is permissible. Additionally, it is important to ensure the involvement of lay people in an open process, so that ethical assessment is not reserved for experts in a closed forum. Finally, it should be ensured that the ethical assessment is of specific applications of genetic engineering and not simply of more abstract questions of principle.

This points to procedural standardisation, which, in relation to specific statutory rulings on the use of genetic engineering, requires that:

1. an ethical assessment is undertaken;
2. this is done on the basis of formulated ethical considerations; and
3. with the involvement of lay people in an open process.

2.2 Different actors

There are many actors involved, and these may have a direct research or financial interest in biotechnology, or be affected in a less direct fashion, or have an interest based on a more

general viewpoint. These actors may have differing viewpoints and interests in respect of research, implementation, financial exploitation, administration, control, governance, etc. of biotechnology.

2.2.1 Researchers, commercial actors and other affected parties

The **researchers** typically work with basic data and generate information from them. They thus generate expert knowledge, which is often of a technical/scientific nature. One dilemma and point of debate is to what extent researchers can, should or will take an interest in communicating and supplying information about ethical issues in relation to their research.

Other sorts of researchers are interested in the consequences of the utilisation of biotechnology, etc. Examples of such researchers might be ethics specialists, lawyers, sociologists, etc. who, from information about biotechnology and their own or others' deliberations of the consequences which the utilisation of different forms of biotechnology will or may lead to, make assessments of various kinds, including the significance it will have medically and socially; the changes of our standards and values which may be at issue; the control measures and options which will be required, etc., etc. While ethics will relate the application of biotechnology to various ethical principles (see above), sociology will often take an interest in its more concrete relevance to specific groups and for society. Jurisprudence, based on pure scientific research, the opportunities for utilisation, ethical principles and sociological considerations, will be able to arrive at an idea of the extent to which there is a need for democratic processes, control, governance, etc. One might perhaps say that these research areas constitute a sort of metascience, which employs some of the raw materials from the other sciences.

Commercial actors will be interested in financial exploitation of biotechnology. This applies, for examples, to farmers, fishermen, food producers, seed producers, etc.

Affected parties can be a number of different groups. One of these will be patient groups, who often press for research and utilisation. Another will be environmental groups and other interest groups, who often remain relatively critical of the utilisation of different forms of biotechnology. Thus, among the affected parties, there will be many heterogeneous and, to some extent, conflicting interests.

2.2.2 Decision-makers and administrators

Based on information they receive, decision-makers, including politicians, will make the political judgement of the extent to which democratic processes, control, governance, etc. should be implemented, and, based on their political assessment, the form to be considered desirable. In other words, they will be selecting which tools to use from the toolbox. Decision-makers can be, firstly, at the international level (UN, WTO, European Commission, EU); secondly, at the national level (governments and parliaments); thirdly, related to different professions (medical associations and trade organisations); fourthly, individual clinics, hospitals, businesses; and fifthly and lastly, the individual person.

Administrators, including authorities, will often develop the expert knowledge and translate it into a concrete utility, e.g. in relation to application, authorisation, policy and transparency. For administrators, there may be relatively large scope for selecting tools in connection with preparation of legislation, the execution of decisions made through legislation, and enforcing the legislation. When the regulation is discretionary in nature, more precise guidance is frequently sought as to which principles the ethical assessment will be based on, and how the more precise balancing of the ethical principles will be made.

2.2.3 The media and the general public/lay people

The **media** play a significant role in information about research, ethical principles, concerns, etc. The media often contribute constructively to debate, but have a tendency to polarise stories so that any balanced view is lost. For example, future hopes can be given such an optimistic slant that expectations are created which have no basis in scientific fact. Or concerns may be (over)emphasised. One of these does not preclude the other, since the media do not need to be consistent in their treatment of biotechnology's ethical dilemmas. In this, they are in contrast with regulation in the area, which must of necessity be coherent and build on an internally consistent position.

Finally, there is the question as to whether there is not, quite besides the above-named actors, a large and important group, viz. the general public. In **the general public** there can be said to be a wisdom which is of great significance to ethical decision-making processes. The long-standing tradition in Scandinavia

for retaining the services of **lay people** in different organisations, councils and boards may be regarded as a recognition of this wisdom. The crux is that experts, including researchers, administrators and politicians, each have their own angle, but that these angles perhaps do not include considerations which large groups of the population wish to see dealt with.

3 Risk assessment - between science and values³

This section has the aim of shedding light on the risks of biotechnology in the "crossfield" between risk and values. The section is based on a more extensive report by Thomas Breck, which is given in Appendix 2. This is interesting, not least in the light of the fact that risk assessment is a key concept in relation to assessment of parts of EU regulation of biotechnology - especially in the foods area - while traditional scientific approaches are changing to become more nuanced, with a higher degree of value-based elements. While scientific risk assessment has traditionally been viewed as relatively unambiguous and therefore a solid foundation for regulation, partly as regards verification, partly as regards creating a homogeneous legal position in the EU, ethical assessments are considered to be more discretionary, and this makes them more difficult to validate and makes it easier for different legal positions to arise in the EU. The difference between the two approaches is, however, not clear-cut.

A glance at the last ten years' debate on biotechnology readily reveals that the risk aspect occupies a prominent position. A large part of the social conflicts played out around biotechnologies seemingly deal with these technologies' inherent potential for danger - their possible risks. How will these technologies affect our health and welfare, our social and cultural identity and the environment? And what precautions should society take to minimise or altogether eliminate these risks?

The word risk is often used to refer to *unwanted* events in the real world, which can be described in terms of their probability and their

consequences. Scientific risk assessments and cost-benefit evaluations are tools employed by technical and financial experts to describe the risk in statistical and mechanical terms. The objective is to provide a qualified basis for political and administrative decisions, for example, on whether a GMO can be authorised for marketing or not.

Such scientific risk assessments have acquired ever-greater significance for societal decisions within modern biotechnology. At the same time, however, criticism has been raised in the public services of these assessments' inadequacy - criticism largely concerning the fact that scientific risk assessments have a tendency to treat risk as a neutral and objective dimension. Risk is not just a question of science, but also of values.

Firstly, scientific risk assessment involves a number of built-in choices of problems, methods and descriptions. These choices can be both well-founded and necessary, so that the risk assessment taken as a whole can provide a result that can be incorporated in a bureaucratic context, but they are never value-free and neutral. **Secondly**, there is a limit to the risk assessment's predication, that is to say the relationship to reality on which it can meaningfully pronounce. Scientific risk assessment has a tendency to include hard and quantifiable aspects and conversely to preclude soft and qualitative aspects of the risk concept.

3.1 Beyond the objective risk concept

In its most common sense, the concept of "risk" alludes to a future unwanted event or situation which one wants to avoid. A risk will often contain an element of unpredictability. We talk about the probability of one or other unwanted event being large or small, and of one risk being greater than another. This is the concept of statistical risk which has gradually

³ The following is based on a report by Thomas Breck, MA Comms and is largely based on the book entitled "Dialog om det usikre - nye veje i risikokommunikation" [Dialogue on Uncertainty - New Paths in Risk Communication], published by Akademisk Forlag 2001, and on the articles "Værdier og risiko" [Values and Risk] by Thomas Breck, Tidsskriftet SALT, 5/2000, "Den ny sociale risikovirkelighed" [The New Social Risk Reality] by Thomas Breck, AVJ-info 4/2001, "Risiko og værdier i GMO-debatten" [Risks and Values in the GMO Debate] by Thomas Breck and Peter Sandøe, Alimenta, 8/2002, and "Sikre fødevarer - også et spørgsmål om værdier" [Food Safety - Also a Question of Values] by Peter Sandøe, Thomas Breck and Karsten Klint Jensen, Alimenta 6/2001. The full text of the report is provided in the appendices section of the Report. Thomas Breck obtained a Masters in communications studies combined with a specialisation in biology in 1988. He has previously worked freelance for the Danish Broadcasting Corporation, as a project manager to the secretariat of the Danish Board of Technology and as an environment affairs consultant to the Danish Consumer Council. He is the author of books on genetic engineering, environmental concerns and risk issues. A PhD research fellow at Roskilde University since 1998, Breck has also for a period been attached to the Centre for Bioethics and Risk Evaluation at the Royal Veterinary and Agricultural University of Copenhagen.

gained a foothold throughout society and which can be immensely useful in many circumstances.

This is how *engineers, economists and statisticians* view risk; as concrete and tangible unwanted events in the real world, which can be described using numbers and probabilities and thereby be made the object of calculations and rational decisions. But precisely because the statistical or objective concept of risk is so widespread, it is important to be aware of its limitations.

In the first place, the concept of statistical risk is concerned with situations where the probability and consequences are known and well defined. Either because there is substantial empirical experience or a well-defined theoretical cause-effect relationship. When the conditions allow, risk assessments can be a splendid instrument on which to base decisions. But many contemporary risks are not simple and well defined. On the contrary, they are often very *complex* and characterised by *scientific uncertainty* as concerns both probability and consequences. This is true, for example, in areas involving hormone mimics and gene modification.

Secondly, the concept of statistical risk presupposes that actors think and act rationally. The reality, however, is that risk is influenced by subjective, cultural and value-laden factors. For example, the individual context means that the risk of driving a car, smoking cigarettes or making a parachute jump is perceived to be more acceptable, since these are our own choices, under our own control. On the other hand, chemicals in food, genetic modification and similar risks imposed by other parties are seen as less acceptable. Psychologists have scientifically proved that risks that are known, self-selected, controllable and fair are seen fundamentally as more acceptable than the opposite type. Added to this is the fact that risk is construed differently by different cultures. For example, Europe and the USA have different views on the risk posed by GMOs to the environment. There is moreover a tendency for scientific experts to prefer risks that can be measured, for authorities to prefer risks that can be regulated etc. Fundamentally, this has something to do with the fact that risk concerns unwanted events, and that the question as to what is unwanted, must, of necessity, be connected with values. It is not least in areas where there is great scientific uncertainty that value-based differences will inevitably play a large role.

The *third weakness* of the concept of *statistical risk* is that it has a distinct tendency to deal only with the risk of mortality. The obvious advantage of this is that all risks can then be compared with each other across both individual and cultural divides. Seen in isolation this is all well and good, but one chooses then to disregard some of the dimensions of the concept of risk which are important for understanding the conflicts surrounding risk that shape debate in society. Aspects to do with scientific *uncertainty*, with a failing *confidence* in science and the authorities and with *value-based* and *ethical* questions.

In summary one can say that the technical/economic approach to risk, in spite of its indisputable merits, also presents blind spots and dead ends, which make it less suited to understanding the many conflicts surrounding risk as characterised by the media and the political agenda in what is referred to as the *risk society*.

To understand the risk society's conflicts it is necessary to adopt a broad, social concept of risk, which includes risk as it is perceived and construed by different individuals and cultures, and which recognises that the conflict between different interpretations and constructs of risks has become a fundamental condition for policy-making. A concept which does not reduce risk to numbers and probabilities, but also sees it as a question of social learning processes and communication. In what one could also call the new *social risk reality*, it is becoming increasingly difficult to refer to risks as something real and well-defined, which can be communicated in an effective and targeted fashion. It is rather a question of contemporary risks occurring, while we discuss them in a mediated process, in which science still plays an important role, but not as a clear and incontrovertible authority. Rather as a store where different social contractors acquire ammunition for their arguments. Arguments which they present to the arena constituted by the media, and where different interpretations of facts and attributed meanings fight over defining the risk and thereby also setting parameters for the political solutions.

3.2 Biotechnology as a risk narrative

Modern biotechnology has from the outset been associated with risk. As early as 1974 scientists warned the rest of the scientific world that the newly discovered recombinant DNA technique poses a potential risk, for example, through

genetically-modified pathogenic micro-organisms spreading outside of the laboratories. A voluntary moratorium was agreed to, until rules were introduced for the use of recombinant DNA. This voluntary halt in the use of genetic engineering is one example of reflexivity and self-policing within the world of scientific research, but it can also be seen as an example of how scientific risk assessment has come to completely dominate the regulation of genetic engineering at the expense of ethical and wider societal perspectives. Biotechnology has become institutionalised in the laws and regulations of society as a potentially risky technology, but the approval of GMOs is almost entirely based on a scientific risk assessment informed by the principle of "if it's not dangerous, it's OK".

The risk assessment has, however, limited powers of predication. The process of hypothetical questions and answers is structured as so-called decision trees of the type "if yes, go to x" and if no, go to y". In this way, the authorities' expert advisers can ensure that all the avenues are covered and the correct questions for the authorisation procedure are asked. If none of the questions on these lines produce a negative answer, an authorisation will be granted. The risk assessment does not, however, take account of knowledge that is lacking, i.e. situations we are unaware of or cannot envisage. In this way, the need for a clear answer calls for the risk assessment to deliver the whole answer, by which it has been obliged to provide a more certain answer than it is in a position to. In order for a risk assessment to be viable in a bureaucratic, regulatory context, the complex realities have to be reduced to something simpler and more tangible. This does not mean that risk assessments are useless, just that they have limited validity.

It is here that the risk assessment loses its status as a neutral instrument for measuring and balancing probabilities and impacts, and becomes itself a contributor to construing conceptions about the nature of the problem. By accentuating the significance of certain factors and playing down others, experts make a series of choices, which might be well-founded enough, but are never value-free. It is crucial for the validity of the risk assessment that these choices and uncertainties are clarified. When a risk assessment is used in a political, regulatory context, however, the opposite often occurs, namely that the choice and uncertainties are played down in favour of an absolute assertion about safety. The risk assessments

then come to appear as the absolute truth and a guarantee against unwanted risk, which they can never be. If unexpected and unforeseen events occur all the same (as happened in the BSE case), both the risk assessments, and the scientific institutions and experts which perform them, lose the confidence of the general public. There is therefore a need for a change in society's use of scientific risk assessment which allows for the scientific uncertainty of that risk assessment.

There are certainly two different ideas of what a reflexive approach to risk assessment of this nature might look like. One technical/scientific and one democratic. The *technical/scientific approach* revolves around the idea that science will become better at assessing risks with vanishingly small probability, but potentially huge consequences in relation to, for example, complex ecological systems. The intention is to incorporate qualitative considerations into the quantitative risk assessment. In this way, one can, as it were, operationalise the use of the precautionary principle, but keep it within a scientific context. The alternative is a *democratic approach*, which seeks to create greater openness about the use of risk assessments - especially the uncertainties and choices associated with them. Additionally, the aim is to include citizens and other non-experts in the process sufficiently early on so that the problem, which the risk assessment is to shed light on, has not already been finally formulated.

Accompanying this necessary discussion of the capacity of risk assessments to predict reality, there is, as stated, another discussion, which deals with the *values underlying the risk assessment*. The main assertion here is that risk assessments are not, and can never be, suited to encompass the value-related questions underlying the entire GMO debate. The challenge therefore consists in breaking the dominance of risk in the regulation of GMOs and to make way for more value-based objections. The view is that the risk aspect may indeed be important but is far from the most interesting aspect of biotechnology. Indeed, the technique raises a series of fundamental ethical and societal questions. About respect for life; about needs and welfare; about sustainability and the need for a more holistic outlook on the relationship between man and nature; and about alternatives to centralisation and increased efficiency and productivity. Fundamentally, it is a question of which values should characterise future food production. There is a conflict

between different world views and between alternative views of humankind's and society's problems and needs. What is immediately apparent here is that the majority of GMOs that have come to market so far are, at the value-level, tightly bound up with the productivity paradigm that has characterised industrialised agriculture over the second half of the last century. In other words, increased volumes and productivity, a faster pace and cheaper products - improvements, which have occurred at the expense of the environment, animal welfare and social sustainability. Some believe that this conflict will change with the second generation of biotechnology products, which concentrate precisely on qualitative improvements, but this is far from given.

The conclusion is that even though biotechnology raises questions about both values and risk, it is symptomatic that public debate revolves almost exclusively around risk. At the same time, the dominance of risk in regulation is a factor in delimiting the objections which can legitimately be raised. Since risk is the only recognised yardstick, one must either assert the dangers of biotechnology - or put up with being ignored. But this trivialises the debate on both risk and values. It is important for the reputation of biotechnology, for the public's confidence and for public debate to make way for a new reflexivity, which must encompass both the value of risk assessment and the values underlying risk assessment.

3.3 The communication of risk as a dialogue about uncertainty

Under the auspices of the FAO/WHO, work is currently being undertaken to create international standards for *risk analysis* in the foods area. In this connection a model has been set out for what might be termed an "archetypal risk analysis" consisting of three steps: *Risk assessment, risk governance and risk communication*. Risk assessment is the scientific part, in which the problem is delineated and the risk described in objective terms in terms of probability and impacts. Risk governance is the term for the political part, where the societal benefits and drawbacks are balanced against each other and the safety levels are determined. Risk communication is the term for the process in which the result of the foregoing process is communicated to citizens or consumers, in the form of a threshold value, dietary advice, hazard labelling and so on. This tripartition is problematical, inasmuch as it presupposes a sharp delineation between the scientifically

objective level (risk assessment) and the political level, where values are introduced (risk governance). As already stated, the reality is

completely different.

Firstly, there is rarely one, unambiguous description of the risk. Scientific risk assessments cannot be neutral, but depend on perspective and are a matter of interpretation. Moreover, they are based on a number of assumptions and are thus representations of reality, but are not reality itself. Many of the risks that typify the risk society are characterised precisely by our lack of knowledge about the relationship between cause and effect - this is true of, for example, BSE and genetic engineering. In these areas, risk assessments become political, and the "scientificism" of matters political follows from a politicisation of matters scientific. This contributes to blurring the sharp divide between scientific risk assessments and political risk governance.

Secondly, risk management has become fragmented. It is not a matter of offsetting costs and benefits, as in a well-structured activity, but often rather unstructured and decentralised risk governance under the influence of many different actors and interest groups who each consider their balancing (read 'their values') to be correct and appropriate in the context. There is in the public sector a battle to define and organise risk and its significance - *risk entrepreneurs* propound and refute others' risk assertions.

Thirdly, risk communication is not a mechanical work of translation, where the message, e.g. a warning, a threshold value and so on, is transferred to the target group as efficiently as possible so that it can then act on the message. Risk communication these days is more than the communication of risk; it involves extensive interpretation and debate about risk as propounded by different actors with demands for specific political solutions and consequences, since whoever controls the definition of risk, also determines which solutions are relevant in the context. Risk is construed, so to speak, by the way in which it is communicated, and one cannot distinguish between the real (objective) risk and the perceived (subjective) risk, where science and values are intermingled and where scientific arguments can be difficult to differentiate from politics and power. The arguments are typically taken from the scientific domain, but there is more to do than produce, set out and interpret the results. This is not a case of a

classic conflict between lay people and experts, since there are both lay people and experts on both sides of the conflict - and they are fighting for legitimacy.

The conclusion for this new picture of risk - this new social risk reality - is that there is a need for new ways of addressing the issue of risk in society and new ways of making decisions within areas that are characterised by scientific uncertainty, by conflicts and opposing interests. There is a need for a new concept of risk communication - one that dispenses with the notion of effective communication. It is important to enter the process as early as possible, and the ideal must be to create parameters for a meaningful public discussion of risk, by ensuring that the relevant actors and interested parties are involved in the formulation of problems and strategies for solutions. This constitutes a major challenge for the authorities that deal with risk communication. The task will be to ensure that the process is as fair, open and transparent as possible, to ensure that all parties are heard, that no important arguments are ignored, etc. In other words the authorities will become a sort of procedural consultant on the risk issue. An important objective for democratic and dialogue-oriented risk governance must be to open up the parameters for legitimate objections that would also comprise wider ethical and societal issues.

PART TWO

REGULATION OF BIOTECHNOLOGY AT INTERNATIONAL AND NATIONAL LEVEL

- Regulation - overview
- Analysis of the regulatory picture

4 Regulation - overview

The following section outlines regulation in the field of biotechnology. The aim is to provide an overview of the current status of regulation in order to localise the description of "tools" within a legislative framework. First, in Section 4, we provide examples of international regulation which reflect some of the ethical principles for which consensus has been reached in prescribing these as universal standards - at a global level, and at the level of the Council of Europe and at EU level.

4.1 International regulation

Since the 1970s a number of attempts have been made to formulate fundamental ethical criteria for regulating biotechnology. In the following we will be discussing some of the main criteria that have been established. The examples are concentrated around human health, GMOs and foods, but we have also included examples covering environmental issues and human rights issues.

The following examples represent regulation in which an attempt to incorporate ethical concerns is in evidence.

The *UN's Universal Declaration of Human Rights* and the *European Convention for the Protection of Human Rights and Fundamental Freedoms* exemplify the attempts to lay down universal normative precepts for fundamental ethical issues.

The Aarhus Convention on Access to Information, Public Participation in Decision-Making and Access to Justice in Environmental Matters (the "Aarhus Convention") from 1988 affirmed "the right to the environment"; not as a material right, but as a number of judicial or formal rights, including the right of access to environmental information, public participation in decisions on specific activities, and right of complaint and of access to judicial proceedings - for non-governmental organisations also.

The *UNESCO Declaration* of 1997 concerns the human genome and human rights and proclaims, among other things, that the "human genome underlies the fundamental unity of all members of the human family as well as the recognition of their inherent dignity and diversity". It goes on to assert that "that dignity makes it imperative not to reduce individuals to their genetic characteristics and to respect their

uniqueness and diversity". Finally the Declaration prohibits financial gain from the human genome in its natural state, and affirms that the benefits of advances in the technologies shall be made available to all, and that freedom of research is "necessary for the progress of knowledge".

The Cartagena Protocol from 2000 concerns biosafety and recalls the UN Convention on Biodiversity from 1992. The Protocol prescribes rules for international trade in living, genetically modified organisms (LMOs). The rules cover risk assessment and risk governance for the purpose of protecting human health. The Protocol also contains rules on "handling, transport, packaging and identification".

The *Codex Alimentarius Commission* was created jointly by the FAO/WHO to develop global food standards. Two committees prescribe general guidelines on risk analysis and labelling of genetically modified foods.

The mission of the *WTO* is to develop a multilateral system of trade, the aim of which is to lower customs and trade barriers, and to abolish discrimination in international trade. The WTO has pledged to work for sustainable development and protection of the environment. Article XX of the GATT agreement and the SPS agreement cover all sanitary and phytosanitary measures that might impact on trade between nations and prescribes, for example, that measures may be introduced in contravention of the principle of non-discrimination if these are based on the precautionary principle. In cases of scientific uncertainty the Member States are permitted to adopt measures that must be based on pertinent scientific information. Since ethical concerns are difficult to document and might be perceived as a paving the way for ulterior national interests that might obstruct the WTO's mission to promote international trade, it is difficult to take account of these concerns. However, the so-called "Shrimp-Turtle Dispute" has eased the constraints on what constitutes an "exhaustible natural resource". The Trips Agreement on trade-related aspects of intellectual property rights also contains a provision that Member States may exclude from patentability inventions contrary to *ordre public* or morality or in order to protect human, plant or animal life, or in order to avoid impacts seriously prejudicial to the environment.

4.2 The Council of Europe

The *Convention on Human Rights and Bio-medicine* from 1997. The Convention prescribes a number of minimum standards with which each Member State must comply, while their national legislation and practice may offer greater protection of the individual than that prescribed by the Convention. The main purpose is to protect individuals against exploitation arising out of treatment or research. The article on purpose and object indicates that the "parties to this Convention shall protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to the application of biology and medicine". The next article affirms that "the interests and welfare of the human being shall prevail over the sole interest of society or science". The Convention also makes provisions for equitable access to health care; for professional standards; for consent and protection of persons unable to consent; for genetic heritage and for scientific research. An Explanatory Report is provided as a supplement containing comments on the text of the Convention. Furthermore, a number of protocols have been ratified with a view to developing, in special fields, the principles contained in the Convention, including a supplementary protocol prohibiting reproductive cloning of human beings.

COMETH. In connection with the Council of Europe's work on bioethics, a provisional bureau known as COMETH (European Conference of National Ethics Committees) has been appointed to promote cooperation and network formation among representatives of a number of national bioethics committees. COMETH organises conferences for its affiliate committees on general and/or topical issues in the field of bioethics.

4.3 The EU:

Regulations drawn up under *EU auspices* include a biotechnology patent directive, a system for regulating approval of clinical trials on medicinal products for human use, and regulations to provide a framework for trials and marketing of GMOs and novel foods. In addition there is the EU Charter of Fundamental Human Rights; EU-US Biotechnology Consultative Forum, the European Commission's policy paper on life sciences and biotechnology, and the work of the EU ethics group - EGE - which reveal that efforts are now being made in the EU to incorporate ethical concerns at a more general and fundamental level.

The *Patent directive* on protection of biotechnological inventions from 1998 is designed to ensure effective, legally harmonised protection of patents and in so doing to serve to encourage innovation and promote investment in the field of biotechnology. The directive contains articles that prescribe restrictions based on ethical concerns. According to these, inventions may not be patented if their use in industry would be against *ordre public* or morality. Examples include processes for cloning human beings; processes for modifying the germ line genetic identity of human beings; use of human embryos for industrial or commercial purposes, and processes for modifying the genetic identity of animals which are likely to cause them suffering with no substantial medical benefits to man or animal, and also animals resulting from such processes. Moreover, the directive stipulates that the Commission's ethics group - EGE - is to assess all ethical aspects of biotechnology.

4.3.1 The authorisation system for medicinal products

Council regulation on medicinal-products 2309/93/EEC

This regulation lays down procedures for centralised authorisation of medicinal products in the EU. It prescribes community procedures for the authorisation and supervision of medicinal products for human and veterinary use and calls for the establishment of the EMEA. According to the centralised procedure, marketing applications are to be submitted to the EMEA, a European agency for the evaluation of medicinal products. The EMEA selects one of the Member States as a rapporteur for the application. The Member State's competent authority verifies the documentation submitted in support of the application, while a scientific committee under the EMEA assesses the application itself. The EMEA grants a Community marketing authorisation which applies in all EU Member States (if the application is authorised).

All medicinal products derived from biotechnology, including those derived by genetic engineering must obtain an EU product authorisation in accordance with the provisions of the EU regulation on medicinal products. National clinical trials preceding an EU authorisation must observe the rules laid down in the Declaration of Helsinki, which means, among other things, that they must be assessed by a scientific ethics committee.

Directive on medicinal products for human use 2001/83/EEC

The directive on medicinal products for human use comprises community code for how national government authorisation of medicinal products is to be implemented. Once one Member State has carried out an assessment of a medicinal product and issued a marketing authorisation, the same product must be authorised according to a more rapid and straightforward procedure in the other Member States in which the manufacturer wishes to market the product. If a Member State disagrees with the marketing authorisation granted by another Member State the matter may be brought before the CPMP (Committee for Proprietary Medicinal Products) attached to the EMEA.

Directive on clinical trials on medicinal products for human use 2001/20/EC (GCP Directive)

This directive fleshes out the ethical principles with specific instructions regarding the components of a scientifically-based ethical assessment. The purpose is to rationalise the procedures involving documentation and administration required for conducting clinical trials, and also to ensure patients of the same protection in all EU Member States. This is what is often referred to as a "minimum directive" in that it is only as prescriptive as the Member States themselves deem necessary for the purposes of protecting human subjects in clinical trials. Before clinical trials may commence a number of criteria must be satisfied, including the weighing of predictable risks and drawbacks as regards the therapeutic benefit for each trial subject and or society as a whole; respect for the trial subject's right to physical and mental integrity and right to personal privacy, and the obtaining of informed consent and permission to withdraw such consent. In Denmark, both the scientific ethical committees and the Danish Medicines Agency are each independently responsible for authorising every application. As a basis for conducting inspections, a European database is to be established to which the Member States' competent authorities are to have access. Inspector visits to selected clinical trials are thus prescribed as a duty. In this directive the EU has drawn attention to ethical criteria.

Openness and co-determination

The authorisation system is founded on the requirement that the rules concerning expert evaluation as set out in the directive on medicinal products are to be adhered to in both cen-

tralised and decentralised procedures. The rules regarding good clinical practice promote self-determination and autonomy for trial subjects and thereby also underpin the principle of openness and transparency. However, this openness applies only to trial subjects specifically and not to the general public. In the field of medicinal product evaluation no tradition exists for publicising applications for marketing authorisations with a view to conducting a public consultation. This may be ascribed to interests in protecting business secrets and researcher rights. The GCP Directive now comprises rules regarding establishment of a Community database with a view to publicising extracts from applications and the evaluation procedure, including, in particular the publicising of adverse effects, though these data are to be made available solely to the competent authorities in the Member States. As such, openness and transparency is ensured for none other than the trial subjects and the competent authorities.

4.3.2 EU authorisation system for GMOs, plants and foods

A recurrent theme is that the Member States are to employ risk assessment and the precautionary principle when considering applications for deliberate release and marketing authorisations. In connection with notification a public consultation must be held, and consumer autonomy must be assured by means of provisions regarding labelling.

Directive on deliberate release 2001/18/EC

The directive on deliberate release lays down the rules for environmental and health evaluation of all genetically modified organisms that are to be released into the environment. All GMOs contained in products sold on the market within the EU must therefore undergo environmental assessment in pursuance of the principles in the EU directive on deliberate release. Authorisations for deliberate release apply throughout the EU. However, the environmental provisions apply solely to LMOs.

If a GMO is used in a food product or a medicinal product it must be authorised for use as such in conformance with the Council regulation on medicinal products (2309/93). In such cases the environmental assessment will be an integral component of the product authorisation, though still in accordance with the principles of the directive on deliberate release. All the rules concerning authorisation of GMO-

based products, including plants, foods and medicinal products have undergone total harmonisation.

The regulation on novel foods 258/97 prescribes requirements for authorisation of novel foods, including GMO-based foods. The regulation also lays down community code for authorisations and the general principles governing labelling. These provisions ensure that consumers have access to the necessary information once the product has been placed on the market.

Openness and co-determination

The directive on deliberate release prescribes that once an application has been received by the competent authority, that authority must publicise it with a view to conducting a public consultation.

Procedure for authorisation of GMO-based products

The actual procedures for authorisation of a GMO-based product to be placed on the European market are relatively consistent with regard to plants, foods or medicinal products. Assessment of the risks to human health and the environment is performed by one of the Member States - either the primary applicant Member State or one appointed through a centralised procedure. The application is then forwarded via the European Commission to the other Member States who make their own assessment and recommendations regarding the application. This procedure forms the basis for a vote on the application in the respective official committees for the individual areas: The committee for deliberate release, the standing committees for foods and for medicinal products for human/veterinary use. If the official committee rejects the application, this is then passed on for a final ruling by the Council of Ministers. If the application is approved, a marketing authorisation is granted that applies throughout the EU.

4.3.3 Other EU regulation, etc. The EU Charter of Fundamental Rights

Proclaimed by the European Parliament, Council and Commission in 2000, the Charter emphasises that the Union is founded on indivisible and universal values of human dignity, freedom, equality and solidarity; on the principles of democracy and the rule of law. It contributes to the preservation of these common values while respecting the diversity of the cultures and traditions of the peoples of Europe, as well as the

national identities of the Member States and the organisation of their public authorities. To this end, it is necessary to strengthen the protection of fundamental rights in the light of changes in society, social progress and scientific and technological developments by making those rights more visible in a Charter. The prohibitions cover issues such as eugenics practices, making the human body and its parts a source of financial gain and the reproductive cloning of human beings.

EU-US Biotechnology Consultative Forum

This body was appointed in 2000 by the then US President, Bill Clinton, and the President of the European Commission, Romano Prodi. The Forum is made up of an independent group of experts whose task it is to issue a joint assessment of a range of complex problems arising in connection with the application of modern biotechnology in agriculture and the food industry. The assessment report comprises recommendations concerning mandatory risk assessment, a number of grants for independent risk research, etc.

The European Commission's communication, Life Sciences and Biotechnology - a Strategy for Europe from 2002 (COM 2002 27 final) (The European Commission's Policy Paper) proposes a coherent strategy for biotechnology aimed at formulating responsible, science-based and people-centred policies on an ethical foundation. The European Council of Ministers has ratified this strategy. An action plan in support of the strategy comprises an overview of various action areas in which concrete initiatives are to be implemented. The strategy emphasises that the development and application of life sciences and biotechnology must be pursued with respect for the fundamental values recognised by the EU in the Charter of Fundamental Rights. The strategy also stresses that scientific and technological progress will continue to raise new ethical and social questions, which should be tackled proactively on the basis of an open and broad debate. The action plan also indicates a number of action areas with a view to strengthening the incorporation of ethical concerns, including information and debate, the elaboration of ethical guidelines/norms and a strengthening of the EGE.

EGE - The European Group on Ethics in Science and New Technologies

EGE is an independent, pluralistic and interdis-

disciplinary authority appointed to advise the European Commission on ethical issues concerning science and new technologies. It consists of 12 members, all of whom have been appointed for their expertise and personal qualities, and the group represents different disciplines, including the health sciences and natural sciences, ethics and theology, and law. Members are appointed by the Commission for a term of four years, which may be renewed once. The group publishes Opinions, either on its own initiative or at the request of the Commission. The European Parliament and Council of Europe may draw the Commission's attention to questions they consider of major ethical importance. For the purposes of preparing its Opinions, the Group holds working meetings, invites experts to take part, initiates studies and organises public Round Tables. If an Opinion is not adopted unanimously the Group must account for any dissenting positions.

4.4 National regulation in the field of health

The following presents a kaleidoscopic view of regulation in the human health area. The purpose is to provide an overview of areas in which broad agreement has been reached on the need for regulation, as well as significant differences between leading EU countries with regard to the intensity and content of their regulation.

Medically assisted procreation is a classic example of "first generation" legislation in the field of biotechnology relating to human health. At the same time, a number of countries exhibit relatively comprehensive regulation, though with a relatively large degree of variation in the method and intensity of regulation. The Council of Europe's Convention on Human Rights and Biomedicine contains only few and modest provisions regarding medically assisted procreation (Art. 14). These focus on non-selection of sex except where serious, hereditary gender-related disease is to be avoided.

a) Consensus areas comprise:

- access to medically assisted procreation restricted to married couples and co-habitees;
- services in medically assisted procreation to be offered solely by clinics and/or persons with a special licence to do so;
- a licence or qualification to provide medically assisted procreation to be granted solely with regard for the principle of *non-commercialisation*; and

- *gestational surrogacy contracts* to be regarded as standard as unenforceable.

b) Areas of dissent comprise:

- access to insemination and IVF by single women and lesbians;
- donation of eggs and fertilised eggs; the legal force of gestational surrogacy contracts; and
- the method whereby the quality of such services may be assured.

Genetic testing represents an area in which regulation is less comprehensive. Regulation of genetic testing is centred on protection against predictive genetic tests "imposed" by external agents, especially employers and insurance companies. This provision is set out in the Council of Europe's Convention on Human Rights and Biomedicine, Art 12. The issue is being deliberated at the EU level generally. EGE, the European Group on Ethics, published a report (*Genetic Testing in the Workplace*) on the issue in 2000. In certain countries the provisions in national regulation are more comprehensive. Norway, for example, has provisions on genetic testing, and Denmark has in special legislation from 1996 laid down provisions concerning the collection and utilisation of health information in connection with employment with the purpose of protecting the right to privacy and integrity.

Gene therapy is an area subject to limited regulation. Where regulation does exist it is usually centred on the difference between gene therapy involving human somatic cells and gene therapy on the human germ line. The issue is referred to in Art. 13 of the Convention on Human Rights and Biomedicine. In the EU biotechnology patents directive, gene therapy on the human germ line is given as an instance in which patenting would be against *ordre public* (Art 6 (2b)) National provisions concerning, for example, prohibitions against gene therapy on the human germ line also occur.

Biobanks represent one of the new areas that have begun to attract regulatory interest. One of the central issues concerns the extent to which the use of biological materials for purposes other than that for which they were obtained (e.g. research) should be subject to express consent (opt in) or whether it is sufficient that no express dissent has been voiced (opt out). In national regulation specific regulations concerning biobanks are (as yet) relatively rare, but the issues will often be covered indirectly by general rules concerning data, etc.

A recent, striking example of direct regulation came with the advent of an act on biobanks in Iceland in 2000. The purpose of this legislation was to authorise the collection, storage, handling and utilisation of human biological specimens in such a way that confidentiality is assured. The issue is currently being discussed in a large number of countries and further regulation will thus conceivably appear on the agenda in future.

Biomedical research represents a classic area for regulatory efforts - albeit more in the nature of soft law. The Declaration of Helsinki has been heavily influential in the formulation of international standards. The Convention on Human Rights and Biomedicine contains requirements regarding professional standards (Art. 4); rules of consent (Art. 5 and others); a general rule that scientific research shall be carried out freely subject to the provisions of the Convention and other legal provisions ensuring the protection of the human being (Art. 15); and special conditions governing the protection of persons undergoing research (Art. 16). In national regulation we also often find regulation designed to ensure scientifically-based ethical assessment of biomedical research projects.

Research on embryos was one of the most controversial issues to emerge in "first generation" regulation in the field of biotechnology. Disagreement on the extent to which research on embryos should be permissible is reflected in an exceedingly vague general rule in the Convention on Human Rights and Biomedicine, which simply states that the law - where the law sanctions such research - shall ensure "adequate protection of the embryo" (Art. 18). However, this rule is followed by an explicit statement, according to which "the creation of human embryos for research purposes is prohibited." At EU level also, we find in one notable respect a provision regarding human embryos, that is, the biotechnology patents directive, which contains a specific prohibition against the patenting of inventions involving the use of human embryos for industrial or commercial purposes (Art. 6 (2c)). In the national regulation the legal position on embryonic research varies considerably.

Cloning, like medically assisted procreation, bears on the most fundamental and sensitive of considerations, in that it confronts the basic premise of human conception. In its declaration from 1997 UNESCO asserts that the reproductive cloning of the human being is to be regar-

ded as a practice in violation of human dignity. In its supplementary protocol to the Convention on Human Rights and Biomedicine, the Council of Europe prohibits cloning, i.e. any intervention that attempts to create a human being that would be genetically identical with another human being either living or deceased. At the EU level the patents directive (on the legal protection of biological inventions) contains a prohibition against the patenting of processes aimed at human cloning for example. The national regulation in a large number of countries contains a provision prohibiting cloning.

Stem cell research represents the latest in a series of regulations on biotechnology, and is the object of much controversy. The Convention on Human Rights and Biomedicine contains no special provisions regarding human stem cell research, as this was not on the agenda at the time of its formulation. There are no EU directives or similar on research on stem cells, but the issue has attracted widespread interest. In May 2002 the EGE published a study on the patenting of inventions related to human stem cells. At the national level stem cell research is generally not the object of specific regulation. Of particular interest is the new legislation in the UK that now authorises stem cell research subject to fulfilment of a number of conditions.

Transgenic animals and xenotransplantation are the object of special interest because they represent a "crossfield" between ethics concerned with human health for both individual patients and in relation to the risk of epidemics, and ethics in relation to animal welfare. Within the EU the xenotransplantation issue is being followed closely, but no directives or other provisions exist for the area.

4.5 The international picture and differences in the intensity of national regulatory activity

International provisions in the area of human health are centred chiefly on four principles:

- a) non-commercialisation (regarding the sale of body parts and restrictions regarding patentability, etc.);
- b) non-discrimination (e.g. non-selection of sex and in relation to genetic heredity);
- c) autonomy (e.g. rules of consent and the right to know); and
- d) the prohibition of reproductive cloning and gene therapy on germ cells.

At the *national* level there is a much variation in the extent to which any actual legislation is applied nationally, and hence how binding the obligations are on which regulation is based. If we look at "first generation" regulation of medically assisted procreation, etc. we can identify the following models:

Laissez-faire means that there is no legislative regulation or only very limited legislation or other form of regulation. This model is found in Italy for example, where it applies to the regulation of medically assisted procreation and other areas.

Liberal attitude means that legislative regulation (hard law) exists only to a limited extent, but that regulation is in operation through professional standards or similar (soft law). This model is found in the UK for example, where it applies to medically assisted procreation (and other aspects of health regulation).

Cautious legislative regulation means that relatively well-developed regulation exists, also in the form of hard law (in some cases in the form of framework legislation). This model is found in France and Scandinavia for example.

Prohibitive legislation means that full legislation exists, and is focused principally on prohibitions and punitive measures. This model is found in Germany and Austria for example.

Thus we find that there are different reactions in the different countries to what the relationship between "ethics and law" should consist of. The advantages and drawbacks of the different models are discussed in Chapter 8.

5 Analysis of the regulatory picture

In the following we analyse the state of the law as regards ethics in regulation in terms of four perspectives. Firstly, "ethics where?" - that is, in which areas regulation stipulates a duty to incorporate or omit ethical principles (coverage) and what scope this affords the individual actors. Secondly, "the ethics of what?", in which we consider the incorporation of ethics in EU regulation in relation to medicinal products and foods respectively in terms of research, clinical trials, deliberate release and marketing. Thirdly, the "ethics of how?" - that is, by what means ethics are operationalised in regulation. Fourthly, "which ethics?" - that is, differences in incorporation and operationalisation of the four ethical principles addressed by the present report. Drawing on this analysis we consider in what areas the incorporation of ethical principles is operationalised more extensively in regulation, and in which areas further incorporation and operationalisation of ethical principles in regulation would seem to be merited.

5.1 "Ethics where?" - coverage and scope of ethical principles

The international provisions in pursuance of which ethical principles are incorporated and operationalised in regulation relate chiefly to two areas.

Firstly, human rights in relation to the human health area. This applies especially to the UN's human rights convention, the Council of Europe's Convention on Human Rights and Biomedicine; UNESCO's universal declaration on the human genome and human rights, the EU Charter of Fundamental Rights in its reference to, e.g. "indivisible and universal values" and the EU Directive on clinical trials of medicinal products for human use.

Secondly, the environment, biodiversity, biosafety and so forth. This applies to the UN Convention from 1992 concerning biological diversity; the Cartagena Protocol on biosafety and international trade in living, genetically modified organisms, as well as the Aarhus Convention on right of access to information about the environment.

In these areas there is thus some degree of obligation to incorporate ethical principles in regulation at the national level.

In other areas the scope for incorporating ethical principles, however, is more limited or non-existent, even. This applies especially to GMOs and foods. The foods standards laid down by WHO/FAO in the Codex Alimentarius, like the EU directives and regulations concerning the marketing of genetically modified products and so forth, contain provisions concerning risk assessment, but leave no or little scope for incorporating ethical concerns in the authorisation procedure itself.

There are, nevertheless, certain "openings" in relation to the directive on deliberate release, the directive on contained use, and the Cartagena protocol on biosafety. Moreover, the requirements regarding labelling and traceability may be said to offer some scope for addressing ethical concerns. Furthermore, the directive on medicinal products for human use contains a provision in which although the authorisation procedure in connection with marketing does not comprise ethical criteria per se, the trials preceding marketing authorisation contain ethical evaluations in accordance with the GCP (good clinical practice) Directive. In this way a link is forged between trials and marketing in such a way that ethical criteria are integrated at an earlier stage, which means that marketing cannot proceed unless certain preconditions regarding ethical evaluation have been satisfied. National scope for incorporation of ethical concerns is in this way limited when it comes to what might be termed "product regulation under EU auspices", since it is based on total harmonisation, in which the rules offer no possibility of ethical considerations - thus making it a contravention of the directives to incorporate them.

The areas of national regulation are chiefly confined to the health sector in the form of medically assisted procreation, genetic testing and gene therapy, research on human embryos, biomedical research and so forth. Ethical evaluations are often integral to authorisation procedures, for example, when it comes to biomedical research projects. Besides these areas, ethics may be included when restrictions are imposed on ethical grounds for what may be approved; as in, for example, a prohibition against reproductive cloning; against employers' requiring predictive genetic testing; against certain forms of medically assisted procreation such as embryo donation, etc. The existence of restrictions of this nature might be referred to in terms of the establishment of a form of "societal ethics" within a given nation, which are subsequently reflected in national regulation.

n the absence of such regulation, the stage is left to the *other actors*, that is, individual professions, scientists, commercial operators and so on. These actors may reach agreement on certain norms for ethical evaluation.

The scope for incorporating ethical evaluations is in this way multifaceted: international ethical principles are formulated to uphold human rights and to maintain biodiversity and biosafety. Against that, a number of EU directives and measures inhibit the incorporation of ethical principles when it comes to GM products, including foods. At the national level ethical principles are centred on human health, while ethical principles concerning the marketing of a number of GM products such as foods are thwarted by the trend for total harmonisation of the EU on this issue. In this way a number of areas are left to other actors, in particular to "professional ethics", "corporate ethics" and "individualist ethics". The issue is discussed in more detail in Chapter 10.

5.2 Medicinal products, plants and foods - ethics

On pages 31 and 32 we have sought to devise a table to indicate the manner in which international requirements regarding medicinal products (for human use) and GMO-based foods are implemented in respect of the criteria governing research and marketing. In the main, the rules aim to ensure consumer protection, while the chief rationale underlying much of the international regulation both as regards medicinal products and foods is to protect freedom of trade in order thereby to lower the barriers that prevent its free flow.

5.3 The "ethics of how?" - different models for operationalisation

Whenever regulation involves the incorporation of ethical principles, the manner in which these are operationalised varies considerably. This applies to the formulation of ethical provisions as broad in scope, discretionary or precise, and also applies to the manner in which ethics are incorporated to regulate either content or process.

5.3.1 Broad, discretionary or precise provisions

International conventions are - almost by their very nature - centred on broad, general provisions, whereby only general ethical principles are emphasised. References to the human health area cite "the precedence of human-

kind", "human dignity", "human integrity", "the diversity of the human family", "respect for the uniqueness and identity of individuals", "freedom, equality and solidarity", and "freedom of research (and thought)". In the area of the environment and foods, reference is made to "biodiversity", "biosafety" and "the right to the environment", as well as "sustainability", "the precautionary principle" and so forth.

These ethical principles set the parameters for concrete, ethical evaluation of a given approach, application or the like, but owing to the "elasticity" of the principles they are open to differing interpretations. In a number of cases therefore, a decisive factor will be the extent to which the concerns embodied by the principles are actually followed through - in other words whether or not they are operationalised.

In national regulation also, we occasionally find expansive statements of intent. This is the case for French regulation, where dignity is a keynote, and for Norway, which besides respect for human worth, human rights and personal integrity emphasises that the medicinal application of biotechnology "shall be for the common good of a society that accommodates all", and that this must be based on "the ethical norms embodied in the cultural heritage of the Western world". Other countries take a more direct approach, dispensing with general preambles in favour of explicit reference to fundamental ethical principles. In the UK for example, it is customary to open with a set of definitions, while Danish and Swedish legislation for example, typically begins by explaining what area the act/statute covers.

When it comes to the details of how to actually implement ethical principles, these have to be translated into more explicit legal provisions. The dilemma is that this will often involve a "quantum leap" from major, sweeping principles on which everyone is agreed, to more precise rules, in which these principles must both be balanced one against the other, and detailed out in relation to discrete concerns. It is therefore small wonder that this localisation process gives rise to major differences in the extent of deliberations and attention to detail.

The dilemma is compounded by the fact that the rule or provision itself may be *discretionary*. This is the case, for example, with the *ordre public* clauses in the biotechnology patents directive and elsewhere, which merely notes that a matter may be contrary to *ordre*

	Medicinal products	Plants and foods
Research	Ethics: EU: Requirements that scientists undertaking biomedical research are to set out the ethical considerations made during project planning, and requirements that the EU evaluation committee assess these considerations.	Ethics: EU: No general provisions for incorporation of ethics. National regulation: No tradition for ethics in evaluations
Clinical trials	Name: EU Dir. 20/2001: Directive on clinical trials of medicinal products. Minimum directive. Ethics: The GCP directive, Art. 6 (ethics committees) The remit of ethics committees is detailed in GCP Guidelines (currently under review) (see Art. 8 of the Dir.).	Name: Dir. 90/219 and Dir. 98/81 on contained use - large scale and greenhouse trials (minimum directive). Ethics: Dir. 98/81 Preamble consideration regarding the requirement that protection must be in place in order to preserve and safeguard the environment and human health.
	NB! Exclusively rules regarding openness for research subjects; no rules on public information or consultations.	Name: Directive on deliberate release 2001/18 (total harmonisation directive) Ethics: Preamble consideration
Marketing	Name: Regulation on medicinal products 2309/93 (distinguishing between medicinal products for human use and those for veterinary use). Ethics: Authorisation is conditional on compliance with the procedure laid down in the directive on medicinal products (GCP). Marketing authorisations may be granted solely on the basis of GCP and the latest standards of the Declaration of Helsinki.	Name: Directive on deliberate release 2001/18 (Plants, but not foods). Ethics: Preamble consideration no. 9 concerning the possibility of incorporating ethical principles in evaluation of applications for deliberate release and marketing applications. Article 9: Public consultation on the application (openness and transparency surrounding the consultation). Article 23: Protection clause (health and environment). Article 29: Consultation of EGE or similar ethics committee.
	NB! Exclusively rules regarding openness for research subjects; no rules on public information or consultations.	
		Name: Novel foods regulation (258/97). Ethics: No reference to ethics.

	Medicinal products	Plants and foods
Consumer protection in connection with marketing authorisations.	Requirement regarding product information (package leaflet to be comprehensible to lay people).	Labelling requirement. Food labelling of novel foods.
Consumer protection post marketing authorisation	Urgent action (EC Treaty Article 30, health/environment/ordre public). Monitoring of adverse effects.	Possibly EC Treaty Article 30, (health/environment/ordre public). Rules regarding labelling and traceability. No specific monitoring of adverse effects (as regards human health).
Other issues post marketing		<p>UN - Cartagena Protocol. Introduces precautionary principle. Informed agreement reg. organisms in transit (AIA - Advance Informed Agreement). Obligatory labelling of GMOs. (Less stringent rules concerning feed and foods).</p> <p>Article 23: Extended obligation to involve the public in decision-making processes concerning LMOs.</p> <p>WTO: GATT Article XX, and SPS agreement: Tendency to recognise environmental concerns and exhaustible natural resources as exceptions to the general rule on prohibition of measures presenting barriers to trade.</p> <p>EU recommendations for regulations regarding implementation of the Cartagena Protocol.</p>

In addition to these the EU directive on patents and the TRIPS agreement contain provisions regarding *ordre public* in connection with the awarding of patents, which comprises both medicinal products and plants/foods.



Areas that impose requirements concerning ethics in evaluations.



Areas for which there are no direct provisions concerning ethics, but which include the possibility of ethical considerations via preambles or provisions regarding purpose.



Areas in which there are no ethical provisions, but which do not stand in the way of the application of general principles.



Areas that do not contain scope for incorporating ethics in evaluations.



Areas that contain principles related to ethical considerations (consumer protection in the form of labelling, traceability, etc.).



Areas in which case law might sanction ethical considerations.

public and morality. In the Convention on Human Rights and Biomedicine, the requirement that research on embryos be made the object of "adequate protection" is also an example of an area in which the intention was to provide discretionary leeway in order to cater for differences in national perceptions.

However, there are also instances in which more precise provisions have been formulated whereby ethical principles are operationalised and acquire prescriptive content.

In such cases the principles tend especially to relate to

- a) non-commercialisation
- b) non-discrimination
- c) prohibitions against human interventions regarded as unethical
- d) protection of disadvantaged groups
- e) risk assessment and labelling

5.3.2 Regulation of content versus process

Ethical concerns may be incorporated in legislative regulation in the form of content-based standardisation, in which the rules indicate expressly what is permissible or prohibited, or in the form of procedure-based standardisation, in which case-by-case evaluations comprise ethical concerns. Content-based standardisation is exhibited in the examples cited above, as well as a large number of national regulations in the area of human affairs (see Part 4). This may be connected with the fact that this is an area ordinarily regulated in the context of family-based legislation and the like. However, scientific research - and to some extent product marketing - are not usually the object of content-based regulation.

Procedure-based standardisation occurs in a number of areas and in different formats, in which the ethical aspect varies. A protocol for authorisation involving the incorporation of ethical concerns is the norm when it comes to trials on human subjects. A typical sphere for such protocols would be scientifically-based ethical evaluation of biomedical research projects. In addition to which there is the regulation of good clinical practice.

Rules concerning public consultation, recourse to raise objections, etc. are also found in the foods area, yet in this context ethical principles are not set out in explicit provisions.

Furthermore, the rules concerning labelling and traceability of GMO-based foods might be classed as a form of procedure-based standardisa-

tion that enables actuation of individualised ethics.

Finally, we find that a proportion of the process-oriented regulation is geared to sustaining a democratic process for tackling ethical dilemmas in biotechnology, including the appointment of ethical councils of various kinds. These democratisation tools are described in more detail in Chapter 6.

When it comes to precise, contextual regulation, the greatest consistency is achieved in operationalisation of ethical principles. The greater the discretionary element, the greater may be the difference between operationalisation and actuation. When ethical principles are incorporated via procedural standardisation this ensures scope and flexibility for ethical evaluation, since an exhaustive tally is rarely made of which ethical principles are to be incorporated - often there will just be a requirement for an ethical evaluation, or for the matter to be brought before an ethics committee such as the EGE. However, this may produce considerable uncertainty as regards which elements are to be incorporated in an ethical evaluation, and how different ethical concerns are to be weighed against each other.

In this way we find that there is what might be referred to as a "quantum leap" from broad principles or procedure-based standardisation to ethical evaluation and decision-making.

5.4 Incorporation of the four ethical principles

Economic and qualitative benefits

The Convention on Human Rights and Biomedicine and the UNESCO Declaration both stipulate that the interests and welfare of the human being are to "prevail over the sole interest of society or science". Also, when it comes to medicinal products we find provisions for ensuring that an evaluation is made of the "therapeutic efficacy" to be derived from the trials forming the basis for authorising the marketing of a product.

In the product area, including GM foods, the provisions permit risk assessment in relation to human health, but do not open up for ethical evaluation of what economic and qualitative benefits might be derived.

Autonomy, dignity, integrity and vulnerability

Human rights criteria and the regular incidence of rules regarding "informed consent" in a large

number of areas may be taken as evidence of incorporation of the ethical principle of *autonomy*. The same applies - albeit more indirectly - in rules concerning foods labelling in the sense that such rules may be understood as an affirmation of the right of self-determination as regards whether or not people wish to consume GM foods. *Dignity and integrity* are classic components in rules of the type that incorporate ethical principles directly, and which moreover often comprise more specific variants, e.g. in relation to the right to privacy (personal data protection), etc. The Convention on Human Rights and Biomedicine contains a large number of rules for protecting especially *vulnerable* groups of individuals. To these should be added the rules comprised by national regulation for the protection of children, including future generations, persons with senile dementia and other vulnerable individuals. Finally, there are a number of rules aimed at protecting the vulnerability of nature, including the environment, biodiversity, etc.

Just distribution of benefits and burdens

Unlike the first two principles, this ethical principle has not achieved the same fixed, prominent status in regulation on ethics in biotechnology. However, isolated occurrences do exist: The UNESCO Declaration proclaims that "advances in biology, genetics and medicine, concerning the human genome, shall be made available to all". The Council of Europe's Convention on Human Rights and Biomedicine refers to "equitable access to health care". The preamble in the Norwegian Act on Biotechnology is a national expression of this commitment. However, the principle also has importance as an ethical concern, that is, as justification for approving GM foods, for example, to the extent that this is to be regarded as a means of helping to feed the world's population. However, this is not presented as an explicit ethical principle underlying any regulation.

d. Openness and co-determination

Openness and co-determination are ethical principles that are increasingly finding general consensus.

In the human health area the Council of Europe's Convention on Human Rights and Biomedicine refers to the importance of promoting public debate on this issue. The EU Charter of Fundamental Rights also proclaims that the Union is founded on "the principles of democracy and rule of law". The European Commission's

communication, *Life Sciences and Biotechnology - A Strategy for Europe*, emphasises the importance of societal dialogue - proactive civic responsibility - and monitoring, as well as scientifically-based regulation. As cited earlier, the Aarhus Convention on public access in environmental matters proclaims a number of rights to ensure openness and co-determination. Similarly, the rules concerning marketing authorisation for GMO-based foods lay down provisions for public consultations. Moreover, all the many ethics committees at the national and the international level have the stated objective of safeguarding openness, dialogue and co-determination. However, it is far from clear what the concept of "co-determination" actually embodies. Public consultation and/or dialogue would appear to be a given component, yet it is difficult to discern what actual influence the consultative response and/or outcome of public dialogue is intended to have.

5.5 Summarising analysis - "gaps in Community regulation"

The overall regulatory picture that emerges is delineated chiefly by four factors.

Firstly: the differences in when ethical principles are promoted and when they are inhibited. In the area of human rights and health international provisions promote ethical concerns in regulation to the extent that it is the duty of each nation, profession and individual alike to address ethical concerns - a duty which comprises the obligation of each nation to operationalise certain ethical principles in its regulation. In the field of GMO-based foods we find that it is chiefly international provisions that inhibit the incorporation of ethical considerations, since, in many instances, total harmonisation prevails such that market interests and the commitment to lowering trade barriers override ethical concerns.

Secondly, the juxtaposition of medicinal products and GM foods. In the area of human rights and health the scope for incorporating ethical principles in regulation would seem to be considerable, especially with regard to clinical trials involving human subjects, since this is ensured by long-standing tradition. In the products area, including the foods area, however, the scope for incorporating ethical considerations would appear to be more restricted, not least because the area is subject to total harmonisation focused on scientific risk assessment and only limited recourse to incorporating

more generalised ethical principles and considerations. The challenges in these two areas therefore set them poles apart. In the last-named area further consideration should be given to whether it would indeed be desirable and feasible to incorporate ethical principles to a greater extent by means, for example, of "gaps" in Community regulation, or, by calling for regulatory amendments.

Thirdly, the "quantum leap" between general ethical principles and the operationalisation required for their actuation. This leap presents problems and often causes agreement on fundamental ethical principles to give way to dissent concerning the details of their interpretation, formulation and actuation.

Along the same lines, there is also the tendency to allow a number of procedural rules to prevail. This has the advantage of flexibility, but often becomes an impediment in that the criteria for ethical evaluation are either inadequate or altogether absent. The challenge lies in filling out this "vacuum" with ethical principles that can serve as guidelines in concrete ethical evaluations and decision-making processes.

Fourthly, that the ethical principles discussed in the present report are not weighted equally in the regulation that exists in the area. The archetypal areas afforded protection are centred on autonomy, dignity, integrity, etc. in the area of human rights and health, and to some extent economic and qualitative benefits, as well as broad-based principles of just distribution of benefits and burdens. However, these have found their way into regulation in the field of GMO products, including the foods area, only by indirect means. Here the focus is on risk assessment and on labelling such that ethics is limited to "isolated ethics". This means that any broader consideration of derivable benefit is not made. The dimension that comprises "proactive civic responsibility", debate and dialogue, openness and co-determination would appear to have increasing influence, though without any clear perspective on how the right of co-determination is to be exercised.

In order to facilitate discussion of how to operationalise ethical principles in regulation it would seem relevant to take a closer look at the "tools" at our disposal. These tools will therefore be the object of a more detailed discussion and appraisal in Part Three.

PART THREE

TOOLS FOR INCORPORATING ETHICAL PRINCIPLES

- Democratisation tools and debate models
- Regulatory instruments
- The toolbox - Check-list

6 Democratisation tools and debate models

The following presents some of the democratisation tools that have been employed over the last ten to fifteen years to establish openness and debate. The main tools covered are: ethical councils, ethics committees, scientific ethics committees, selected debate models, selected specialised ethics committees and joint bodies. The ensuing discussion about the advantages and drawbacks of these resources derives from a combination of analysis work, interviews with various people with experience and expertise in the area, and our personal findings and opinions.

6.1 Ethical councils (debate and advice)

There are now a range of different models for ethical councils and committees in Europe. *France* was the first country in the world to establish an ethical committee; this was in 1983 (Comité Consultatif National d'Éthique pour les sciences de la vie et de la santé). In *Denmark* the Danish Council of Ethics was established in 1989. Ethical councils were established in *Germany* in 2001; in *The Netherlands* in 1999; in *Sweden* (Swedish National Council on Medical Ethics (SMER)) in 1985; in *Norway* in 1991; and in the UK in 1991, with the assistance of private funds, an independent, autonomous ethical council was established, but not, however, based on legislation or government decision. The UK government decided in 1998-99 to establish, instead of an ethics council along the lines of the French or Danish ones, two autonomous councils, each devoted to their own specific field, namely human genetics - The Human Genetics Commission - and the agricultural and environmental area - The Agriculture and Environment Biotechnology Commission. Additionally, in 2000, the Food Standards Agency was set up, with the remit of protecting public health from risks that may arise in connection with food consumption, and in other ways protecting consumer interests in relation to foods, including genetically modified foods.

6.1.1 Nomination and members

The number of members and their backgrounds and representation vary somewhat. The French ethics committee consists of a Chairman and an Honorary President nominated by the

President, plus 39 members. 5 members represent the major religious denominations and are nominated by the President. 19 members are selected based on their qualifications and competencies and their interest in ethical questions. 15 members work in scientific research. There is therefore a high representation of specialist members, including specialists in ethics and philosophy.

The Danish Council of Ethics consists of 17 members, made up of a mixture of specialists and lay people. 8 members are nominated by the Ministry of Health, 9 by the Danish Parliament's committee on the Council of Ethics. The members are nominated for their public commitment to the Council's remit, and they must not be a member of the Danish Parliament, a local authority or a county council. The act on the Danish Council of Ethics also stipulates equal representation by men and women. The Danish model for a council of ethics is characterised by its large proportion of lay representatives.

The German council of ethics consists of up to 25 members, covering the scientific disciplines within the life sciences, medicine, theology, philosophy, sociology and law, along with experts in ecology and economic affairs.

Members of the UK Nuffield Council (ethics council) are nominated by the council itself and consist of various experts, of which around half represent medical and scientific disciplines. There are also experts in ethics and, for example, an anthropologist and a broadcaster. Members of the UK advisory ethics commission, The Human Genetics Commission, are publicly advertised for and selected by the Ministry of Health. Most of the members are experts in genetics, health, politics, law or bioethics, but there are also others from, for example, trade and industry - but no politicians.

The Swedish medical ethics council consists of a chairman, 8 representatives of the political parties and 11 specialist members.

In some countries members serve for a limited period; e.g. membership of the Danish Council of Ethics is limited to a maximum of 2 terms of 3 years, and in Germany members are appointed for 4 years.

Sometimes, there are also provisions for equal representation of men and women, e.g. in the Danish Council of Ethics.

6.1.2 Objective

The French ethics committee is an independent body linked to the ministries of research and health. The committee has an exclusively advisory function, and advises and prepares reports initiated by questions from parliament, the government, an institute of higher education, a public institution or a recognised public research foundation, as long as their main activity is research, technological development, or the promotion or protection of health. The committee can also take up matters proposed by members of the committee itself or by others.

The Danish Council of Ethics has two main functions - an advisory function for legislators and the government and a dissemination and debate-promoting function for the public. To a great extent, the Danish Council of Ethics has contributed to broadening the public debate by arranging public consultations and debates about ethical questions relating to the new technologies within biomedicine. The Council seeks to communicate ethical issues relating to biotechnology and human health to non-specialists.

The German council of ethics is also independent and sets its own agenda and *modus operandi*. The aim is to discuss and arrive at an ethical position on questions raised by new developments in the life sciences, as well as their consequences for the individual and for society. A particular emphasis is given to links with the public domain.

The UK Nuffield Council is also an independent, autonomous ethical council, which, in the absence of a national ethical committee as such, has achieved a position as an important player in the UK and international ethical debate on the new biotechnologies and in the formulation of UK policy in the area. The Council sees it as its task to identify and define ethical questions raised by the developments in biological and medical research, with the aim of responding to and anticipating public concern.

To a great extent, the Danish Ethical Council has contributed to broadening the public debate by arranging public consultations and debates about new technologies within biomedicine. The council seeks to communicate ethical issues relating to biotechnology and human health to non-specialists.

The UK Nuffield Council has published a large number of reports with comprehensive scientific documentation and has, moreover, set up

meetings where ethical questions are examined and reported on with the aim of promoting public awareness and debate. From this basis, new guidelines are often formulated in a number of areas.

The Swedish ethical council is appointed by the government and has the task of shedding light on medical ethical questions in relation to society in general. The council provides guidance to the government and parliament, which includes assessing impacts on the individual and human integrity in relation to medical research, diagnostics and treatment. It functions as a senior advisory body, monitors developments in the area and builds bridges between researchers and decision-makers.

6.2 Scientific ethics committees (authorisations)

In a number of countries there is scientific assessment of biomedical research projects involving human subjects. In the following we will be looking at the following countries in more detail: The Netherlands (CCMO), Sweden (Swedish National Council on Medical Ethics - SMER), Norway (National Committee for Medical Research Ethics - NEM) and Denmark (the scientific ethics committee system - CVK and others).

6.2.1 The committees' composition

The Dutch committee consists of 11 members and 8 experts (deputies). The committee has at its disposal ethical, legal, medical and pharmacological expertise and expertise in nursing. As well as its members, the committee also has attached to it 10 experts with specialist competence in gene therapy, xenotherapy, immunology, embryo and germ line research as well as legal expertise. The committee is served by a secretariat of 9 staff.

The Swedish committee consists of a chairman, 8 representatives of the political parties and 11 specialist members.

The Norwegian committee has at least 9 members and, besides medical competence, has members with competence in the relevant research disciplines and specialist competence in ethics and law. At least one of the medical members has to have clinical competence and the committee must also have competence in genetics and psychology. At least two of the committee's members must be lay representatives. The committee's members are nominated

by the Ministry of Ecclesiastical Affairs, Education and Research following recommendations from the Norwegian Research Council. They are initially appointed for a term of 3 years with the possibility of reappointment.

The Danish scientific ethics committees usually have seven members, i.e. four lay people and three specialists. The committees' period of operation follows the county council elections. The members are nominated by the county council. The lay members are generally county council politicians. Their appointment takes politics into account. The final nomination of the specialists is also made by the county council, but must previously have been approved by the three research forums of the Universities of Copenhagen, Aarhus and Odense and by the Danish Medical Research Council. This procedure is to ensure that the specialists have knowledge of research, e.g. that they are active researchers.

6.2.2 Areas of responsibility

The Dutch central committee controls all medical research involving human subjects in The Netherlands. The committee also supervises the regional research ethics review committees, of which there are several dozen in the country. These local scientific ethics committees (METC) must be approved, and there is a condition that the committee fulfils a number of legal requirements as to its composition and articles of association. The assessment of biomedical research involving human subjects will be made either by a local committee or by the central committee, depending on the type of research in question; e.g. gene therapy and xenotransplantation trials, as well as certain projects involving children, can only be assessed by the central committee, which also advises on trials involving the use of embryos and the human germ line. The central committee (CCMO) also acts as an appeals body.

The Swedish regional research ethics committees assess research projects involving the use of human subjects in biomedical trials. The activity of these committees is not regulated by law and they are appointed on a voluntary basis. In practice, biomedical research projects in Sweden cannot be undertaken without approval by a regional scientific ethics committee. These are primarily based in hospitals and universities.

The Norwegian scientific ethics committee is an independent body, which acts as a "watchdog", information service and adviser at national

level. The committee's job is to be a coordinating and advisory body on research ethics for the regional committees for medical research ethics. Additionally, the committee is required to inform researchers, administration and the public about current and potential research ethics issues in the field of medicine. In each of the country's 5 health regions, local committees for medical research ethics (REK) have been set up using guidelines laid down by the Ministry of Ecclesiastical Affairs, Education and Research, which also nominates the committees' members. The committees are required to vet all biomedical research projects involving human subjects.

The Danish scientific ethics committee system is made up of regional, county-based scientific ethics committees and a central scientific ethics committee. From 1982, the system worked on the basis of voluntary agreement, but since 1992 has been regulated by law. This means that it is illegal to carry out a biomedical research project without permission from a scientific ethics committee. The regional scientific ethics committees assess medical trials involving human subjects, monitor approved trials and participate in ethical debate in the region concerning biomedical trials. The Central Scientific Ethical Committee is an appeals body for decisions made by the regional scientific ethical committees, and this includes disagreement within individual committees or between several committees. The central committee has no competence to issue binding guidelines to the regional committees, but can recommend that they treat certain types of projects using particular guidelines, with the aim, among other things, of ensuring consistent treatment nationwide.

6.2.3 Assessment criteria

For the Swedish committee, it is laid down that it must assess whether the project is scientifically beneficial to undertake, including whether the anticipated benefits from the project outweigh any potential risks which the execution of the project may have for the individual subject/patient. Furthermore, the committee has to ensure that the subject is given sufficient information about the implications of participating in the trial, and to ensure that informed consent for participation is given.

In Danish legislation on the scientific ethical committee system a number of conditions are prescribed which need to be approved before a trial can be undertaken. "In its evaluation, the

committee will take especial care that the risks from the project are assessed, that subjects or their guardians are fully informed about the trial and have provided written consent, that the subject understands that he/she can withdraw from the trial at any time and that he/she is apprised of the project's finances."

Moreover, the law also demands that emphasis be given to scientific standards, in that the committee has to assess whether the trial, in its aims and methodology, meets high scientific standards, and that there are adequate grounds for carrying it out.

This assessment has to be made because it is unethical to include people in a trial which does not have sufficiently high scientific standards.

6.3 Other democratisation tools

6.3.1 Technology councils, including consensus conferences

The Danish Board of Technology and its procedures will be used as a basis for analysis, since it has worked with the consensus conference model over a number of years.

The Danish Board of Technology has the job of promoting awareness of technologies, their potentials and consequences for people, society and the environment; and this includes generating debate about technologies, assessing technologies and advising Parliament and the government on technological issues. It is an independent institution with a board of 10 members and a committee of 50.

Consensus conferences have the aim of including citizens and their experiences in the technology assessment and are therefore conducted as a dialogue between experts and citizens. They normally stretch over 3 days and are open to the public as concerns expert presentations and the consensus panel's questions to the experts. The role of the experts is to inform a panel of citizens about the technology and its implications. The civic panel then jointly drafts a final document which contains a concluding statement and position on the issue. The consensus conference is managed by a planning group, which advertises for and selects a group of 10-15 citizens, summons suitable experts and attends to conference promotion and publicity. On the first day of the conference the experts have the floor, while the second day provides the panel members with the opportunity to put questions to the experts. After that,

the civic panel produces its final document, which is presented and published on day three.

The model for consensus conferences consisting of dialogue between citizens and experts has been adopted in a number of other countries. In the Europe region, consensus conferences have been held on the application of biotechnology in France, Germany, the Netherlands, Norway and the UK. The question is whether it will eventually be possible to envisage holding consensus conferences at the European level, with a panel of citizens from different countries.

6.3.2 Future panel

In connection with extending the dialogue with politicians in the Danish parliament, the Danish Board of Technology has established a future panel of parliamentarians.

The future panel follows, over a number of years, a field of technological development via consultations and other events, and draws up cross-party memoranda on the long-term political potential and challenges in the field.

The future panel is a new concept in Denmark, which makes it difficult at present to discuss its advantages and drawbacks. One can, however, say that the intention is to ensure that politicians have better opportunity for direct dialogue with specialists about issues and problems concerning the future use of technology.

6.3.3 Values workshop - Norway

This workshop is interesting because one of its aims is to establish a dialogue with a specific business sector about the ethics relating to the future development of the business sector. One example was Norway's fisheries in 2020.

The aims included:

- providing a complete and well-founded value-based assessment of Norwegian fisheries;
- mapping out relevant values, so that explicit value choices can be made;
- trying out a new method with reference to structuring ethical considerations as regards strategy choice; and
- engaging in debate on ethics in the fisheries industry and in society.

The strategies included:

- establishing a network, including a working group from Norges Fiskarlag (fisheries union) and other institutions;

- developing scenarios for the fisheries industry towards 2020, according to which four scenarios provided the basis for clarifying ethical aspects of strategic decisions in the fisheries industry;
- developing an ethical matrix for the fisheries industry, in which the ethical values are structured in relation to central ethical principles and affected parties. The matrix is a diagram consisting of rows and columns with a checkbox, called a cell, at each intersection. There was then produced: an ethical matrix, in which the fundamental principles of fairness, dignity and welfare were specified for each affected party and then weighted to arrive at concrete values; an impacts matrix, in which specific options for action were evaluated; and finally, an evaluation matrix, in which numerical values indicate how far the impacts described in the action matrix will result in respect for the specification and weighting of the individual ethical values. On the basis of the evaluation matrix, a final estimation of the options for action is made.

6.4 Cooperation between councils and boards

The distinguishing traits of biotechnologies, in which different areas, actors and decision-makers need to interact, make it expedient to open up new avenues for cooperation.

The following gives examples of such cooperation between councils and boards in Denmark.

a. Biosam

In Denmark over the last 5 years, closer cooperation and coordination has been implemented between councils and boards working with questions of bioethics as related to human health, animals and biotechnology. This cooperation is centralised in BIOSAM, which is a joint body of representatives from The Central Scientific Ethical Committee, The Council of Ethics, The Danish Board of Technology, The Animal Ethics Council and The Animal Experimentation Inspectorate, and which liaises on ethical issues associated with biotechnology research and the application of biotechnology, including cloning and the genetic transformation of mammals.

BIOSAM also contributes to making Parliament and the public aware of new developments in research in, and the application of, biotechnology. The joint body must continually keep Parliament

and the public informed about its work and take the initiative in making the ethical problems surrounding biotechnology the subject of public debate.

Furthermore, BIOSAM cooperates with the interministerial taskforce for biotechnology and ethics (BioTIK), which is responsible for implementing a four-year action plan containing a range of initiatives concerning biotechnology and ethics. The BioTIK taskforce coordinates statutory work in the field on the basis of recommendations from an external BioTIK reference group, consisting of representatives from councils and boards, non-governmental organisations and researchers.

b. The Danish Council of Ethics and the Animal Ethics Council

Two councils, the Danish Council of Ethics and the Animal Ethics Council, have similarly, over recent years, cooperated more closely, by holding joint information meetings. Additionally, a particular joint focus has been directed at the question of cloning. Thus, in 2000, the Danish Council of Ethics published a discussion paper, dealing principally with issues concerning technologies for tissue and organ propagation and the future potential for the genetic manipulation of humans and animals.

c. The Danish Council of Ethics and the scientific ethics committee system

In accordance with the act on the scientific ethics committee system and the act on the Danish Council of Ethics, the Central Scientific Ethical Committee and the Danish Council of Ethics are required jointly to address the more fundamental ethical issues concerning biomedicine. The Danish Council of Ethics' task is to advise the Minister for the Interior and Health, Parliament's committee on the Danish Council of Ethics and the health authorities about ethical matters relating to new biomedical technology and human health. The Council is also required to promote public debate about these issues. Over the past decade or so, the cooperation has resulted in the holding of information meetings in which representatives of the two bodies have exchanged information about the work. Furthermore, in recent years, there has been closer cooperation between the Central Scientific Ethical Committee and the Danish Council of Ethics, which, among other things, has given rise to joint events, in which both bodies have planned and implemented the joint initiatives.

d. Cooperation between the Danish Central Scientific Ethical Committee and the Danish Medicines Agency

The Danish Medicines Agency and the committee system coordinated by the Danish Central

Scientific Ethical Committee operate a parallel procedure for authorisation of biomedical research projects involving clinical trials of non-approved medicinal products. The Danish Medicines Agency grants the final permission for such projects. According to this system of bipartite decision-making competency, it is the Danish Medicines Agency that makes the final decision on any authorisation to commence trials on medicinal products involving human subjects. The Agency's decisions must be made on the basis of a recommendation from the committee system. Given that it is the committee system that has the sole authority to conduct a scientifically based ethical evaluation of a prospective biomedical trial, the committee's recommendation is in effect binding on the Medicines Agency as regards the scientific component of ethical evaluations.

This bipartite decision-making mandate entails liaison, and this takes the form of a coordinating committee of representatives from each of the two bodies. In recent years cooperation between the two bodies has been devoted largely to the EU draft directive on good clinical practice (GCP Directive), in which representatives of both the Danish Medicines Agency and the Danish Central Scientific Ethical Committee participated in the EU talks.

e. Collaboration on gene therapy

In 1999 there was a case in the County of Aarhus concerning a research project involving gene therapy on human subjects as part of a study of the treatment of patients suffering from hepatic cancer.

The "Aarhus Case" revealed the need to establish interdisciplinary collaboration among the authorities mandated to grant authorisations for clinical trials involving gene therapy. Trials of gene therapy involving human subjects involve major environmental, epidemiological and ethical aspects.

In response to this sequence of events a coordinating committee was appointed by the Danish Medicines Agency for the purpose of promoting dialogue among the authorities responsible for granting the various authorisations. The coordinating committee, made up of representatives from the Danish National Board of Health, the Danish Medicines Agency, the

Danish Central Scientific Ethical Committee, the Danish Forest and Nature Agency and the Danish Labour Inspectorate, attends to the authorisation of human clinical trials involving gene therapy.

6.5 Analysis and evaluation of democratisation instruments

6.5.1 Representation of experts and of lay people

Expert representation comprises groups of expert delegates representing the disciplines concerned, e.g. biotechnology, biomedicine, philosophy and ethics, law, sociology and psychology along with other disciplines as required.

The advantages of having such representation are that this provides a means of securing comprehensive and well-founded academic expertise for the advisory and decision-making services rendered by the various committees. In this context interdisciplinarity is crucial, since under this concept the representatives of different disciplines can meet and discuss ethical issues as a means of familiarising themselves with each other's terminology, culture and scientific traditions. This then serves to promote mutual understanding among different scientific domains.

It is essential that the concept of expert representation is not defined too narrowly, and that careful consideration is given to which experts will be the most appropriate, especially with regard to the need to include sociologists, anthropologists, psychologists and other social scientists.

The drawbacks of establishing forums comprised exclusively of experts are that they may have a tendency to become somewhat "introverted" in their choice of issues and mode of discourse. Communication with the public and decision-makers may be hampered by the fact that many academics have no particular tradition for opening their debates up so as to make them accessible and comprehensible to the general public.

Lay representation involves delegations made up as "counterweights" to (academic) experts. The involvement of lay people is already a time-honoured component of the Danish judicial system, the purpose of which is to ensure that the public's sense of justice is reflected in criminal procedure. In addition, the involve-

ment of lay people occurs in public governance, e.g. in central tax administration in Scandinavia. In the consensus conference model the use of lay people may be understood as drawing a parallel with jury service in the administration of justice. The experts are comparable with the witnesses summoned before a court; the panel with the jurors, who, after hearing the expert testimonies, withdraw to formulate their collective response to the conference issues, informed by the presentations of the experts and their own common sense.

The advantages of drawing on the services of lay people are, among things, that they have a confidence-building function, whereby the link with general public opinion and common sense may be sustained. Lay people thus serve to contribute an element of "wisdom", which ensures that account is taken of the opinions and convictions that exist as implicit tenets in the values embraced by a population. This should also be considered in the light of the fact that lay people are perfectly capable of acquiring objective and valid insights and that scientific experts are just as susceptible as lay people to subjectivity and personal factors. Moreover, the involvement of lay people serves a democratic function in that it exercises the principle of autonomy and counteracts the formation of unintended power bases. This serves to establish what might be termed a "bottom-up" element in decision-making processes, just as it ensures dialogue on the issues that the public finds to be important, and ensures that the concerns deliberated are communicated to the public in a way that is comprehensible to the "man on the street", and which thereby contributes to social and democratic learning processes. The subjective and personal factors brought into play by lay delegates will thus be incorporated in consultations on the issues that present themselves for discussion.

Denmark maintains a large body of lay people in its ethics committees - according to a model in line with its long-standing tradition for retaining the services of lay people in the judicial system, in connection with jury service in appeals courts, for example. The findings of consensus conferences have been that ordinary, motivated citizens are capable of acquiring and analysing complex scientific information, and of drawing their own, independent conclusions. The "worldly wisdom" possessed by lay people serves to complement the more abstract and generalising insights of academic experts and thereby contributes to a more balanced

foundation for decision-making than if all decisions were made solely by such experts.

The drawbacks of retaining the services of lay people include the risk that they may become "over-qualified" in connection with their involvement and representative services to expert bodies. A failure to take special account of the fact that the role of lay people is precisely to provide the originally-intended safeguards and to approach the issues from new angles might mean that the values and culture of the academic experts might come to dominate the agenda such that the lay element is at risk of being "held hostage" by expert opinion. It should therefore be ensured that the views held by lay representatives are allowed to evolve freely, and that "down-to-earth" opinions are not compromised. Further problems may arise if extensive lay participation displaces the volume of experts deemed necessary without excessively swelling the ranks of the organisation.

Political participation in debate-generating activities will often be useful; the problem being that politicians tend to be reluctant to get involved at an early stage in issues that may be regarded as "dangerous" or "awkward" to take a public stance on. In relation to ethics committees, one purpose of which is to serve as an advisory function, it is doubtful whether political participation would be of value.

The advantages are that this ensures a "direct line" to the political domain, which in turn ensures that the advisory element dominates, and that the political domain becomes accustomed to discussing difficult ethical issues in greater depth.

The drawbacks may be that politicians run the risk of backing a given opinion prematurely, which again may pose further problems. The risk is also that the political level engages too early in the process, when it may be more helpful if the debate can proceed in the absence of political interests.

One conclusion on the views presented here might be that it is vital to ensure broad interdisciplinary expert representation - possibly complemented by a panel of academic advisers who may be consulted on specific matters - but that there may equally be a need to ensure lay representation, both in the democratisation instruments designed to generate debate, and in ethics committees - whether these serve an advisory or controlling function. This ensures

an open, transparent system, as well as a counterweight to prevent medico-professional and research-based interests from dominating in relation to the mechanisms for protection that may be deemed equally important. At the same time this promotes valuable dialogue between experts and lay people. In this context it is important that lay people are provided with sufficient, readily comprehensible information such that they may render their services on a sufficiently well-informed basis, being apprised of the technical data.

The retention of lay services is often endorsed in relation to debate models proper, which refer to public debate in various forums, etc. However, it is important that the lay contingent and generalised debate are also employed in relation to scientific ethical committee systems in which actual authorisation of biomedical research projects is effected, since these committees do not necessarily consider broader ethical implications involving general societal concerns and regard for future generations. Such aspects may play an important role in connection with deliberations on research projects seeking to employ technologies such as xenotransplantation, stem cell research and cloning of human cells. Deliberations on the broader ethical implications of such projects should therefore be ensured by retaining the services of lay people in scientific ethical committee systems and by incorporation of the debate models proper.

The question of the term in which lay people should serve has also been debated. The fact that it takes time for lay people to familiarise themselves with complex issues speaks in favour of an extended period of service. In contrast, the fact that it may be necessary at times to "inject" fresh opinions and new participants into the debate speaks in favour of a rather more limited period of service. The latter argument would seem to be the more persuasive.

6.5.2 The purpose and role of the committees

It is often emphasised that is of the utmost importance for ethics committees to be independent. Only in this way can they meet the need for information and debate in a way that comprises an objective stance on current regulation and prevailing opinion, even when this is at odds with the position held by government and parliament for example. The UK Nuffield Council has even gone so far as to stress that independence from national government is

important in the light of an evident lack of public confidence in government-appointed advisory bodies. It may therefore be preferable to establish independent bodies of this nature - ideally at the national level - and to furnish them with sufficient financial resources to allow them to act in an advisory and debate-promoting capacity. While some countries have a single, centralised ethics committee and sub-committees to attend to the more detailed particulars, other countries primarily rely on a number of dedicated committees. Similarly, commissions may be permanent or provisional, mandated to generate debate, to advise, authorise or regulate, and assigned a more or less explicit remit.

One essential aspect is to avoid any dispute over authority among the various bodies appointed, and prevent overlap and the duplication of effort this might give rise to. In this respect it is important to establish actively cooperating bodies. This need also emerges from the fact that many of the ethical issues addressed touch on multiple concerns that may need to be addressed by separate committees. The need for interdisciplinarity and cooperation is therefore pronounced.

The difference between the desire to achieve consensus or not is based on a weighing of advantages and drawbacks.

The advantages of consensus would appear to be that the greater the level of agreement presented by a given ethics committee, the greater will be its prospects of bringing influence to bear on the regulators.

The drawbacks are that such a committee will thereby forfeit much of its impetus, since controversial issues and/or principles are usually the very aspects that make consensus difficult to achieve. It may therefore be helpful to furnish the decision-makers with detailed information as to where any dispute might arise, and which ethical principles may be assessed and weighed differently such that the decision-makers will have the best possible basis of information at their disposal to assist their deliberations.

There is also a need to establish cooperation among the various administrative units assigned to address ethical concerns - partly in the form of experience exchange, partly with the aim of ensuring that there is minimal inconsistency within a single area and between one

area and the next. The same issue may arise among regional, local hospital-based authorisation bodies, for example, meaning that practices may vary in different national regions. This coherency would seem appropriate in the light of the fact that local variation should be acknowledged, whereas in terms of equality this may appear less reasonable.

6.5.3 Criteria for ethical evaluation

One of the difficult questions concerns which criteria should determine whether an authorisation is granted or rejected.

The ethical principle of *economic and qualitative benefit* is occasionally comprised by preconditions dictating the balancing of the risks against the benefits of carrying out a given biomedical research project involving human subjects. In addition, we occasionally find a requirement that there must be justification for carrying out a project. However, the problem may be that the decision-making process and the decision-making forum concerned may not be geared to or possess the resources to make a broad and more nuanced ethical evaluation, confining itself instead to a more narrow, scientifically based ethical angle of approach. In the debate models these ethical principles will often be incorporated, despite the fact that they may be challenging to deal with, since it can be inordinately difficult to predict economic and qualitative benefits balanced against any longer term risks.

Autonomy, dignity, integrity and vulnerability are assured in scientifically-based ethical authorisation systems in the shape of the requirement concerning informed consent. However, it is doubtful whether the principles of dignity, integrity and vulnerability will actually be subjected to sufficiently incisive, nuanced and predictive considerations in an authorisation system. *Just distribution of benefits and burdens* are not incorporated in the authorisation system, save for the requirement that there must be justification for carrying out a trial. However, there is often reason to question whether those research projects that do go ahead actually take sufficient account of the needs assessment that this ethical principle represents. In the debate models, this principle can readily be addressed - which it often is, but here too it will often be difficult to document and analyse its use in any detail.

Co-determination and openness form the basis for the debate models in the various formats discussed in the foregoing, and it is encouraging to find that these principles are becoming more widespread all the time and have now also been identified with great emphasis by the EU in the form of a drive for "proactive civic responsibility". However, in the authorisation system the principle of co-determination and openness in decision-making is far from always observed, among other things because the issue of intellectual property rights may conflict with the provision of more extensive information. Greater openness could presumably be achieved without producing any conflict with patent rights and so forth, which would be desirable in the case of any applications that raise more general ethical issues.

7 Regulatory instruments

In the following we outline the functions of regulation and introduce various forms of regulatory instruments. The advantages and drawbacks of the various regulatory instruments will subsequently be analysed and evaluated.

7.1 Regulatory function

Legislation has three primary functions, that is: normative, protective and regulatory:

7.1.1 The normative function

International instruments will to a great extent often be normative in nature in the interests of achieving consensus. Examples of this may be found in the UNESCO Declaration, the Council of Europe's Convention on Human Rights and Biomedicine and the EU Charter of Fundamental Rights (see Section 4 above). Art. 6 of the *ordre public* clause in the EU patents directive also contains a provision that can be characterised as normative. In addition we find that national traditions in some countries contain examples of provisions with a normative quality. The normative component of legislation entails that certain values and interests are emphasised as worthy of protection. Such values and interests might include human dignity, protection against genetic discrimination, prohibitions against germ line interventions, cloning, hybridisation and research involving embryos (after a certain timespan). This function of the legislation is based on a vision that laws may be educational, a means of exercising ethical principles.

7.1.2 The protective function

This function of legislation balances protected values against other interests, and prescribes sanctions for abuse, while it seeks to minimise risk factors for patients and other persons affected by biotechnology and its applications.

Examples include the protection of children born as a result of medically assisted procreation and persons in a vulnerable position such as those applying for a position of employment or for insurance cover, etc. This may produce legislation to ensure that people cannot be legally required to undergo genetic testing, etc. in cases where they are applying for a particular job, insurance, a pension or the like. In this way their "right *not* to know" about their genetic heritage may be protected. Legislative protection may be necessary because informed

consent does not offer adequate protection in situations where there is inequality in status. It is therefore not a question of saying yes or no to genetic testing, but of saying yes or no to a given job or a given insurance policy.

Another example is the function of protecting future generations. This concern is to be regarded as of such importance that it must necessarily be ensured by legislative means, among other things because there can be no certainty that this concern will be observed by those immediately affected. Besides the physical environment the regard for future generations can also be observed by safeguarding the cultural environment, social interactions, etc.

Finally, protection in the form of legislation may be appropriate for purposes of risk minimisation, as exemplified by the precautionary principle.

Many of the areas in which the protection concern is an issue will be those areas in which informed consent does not provide adequate protection, either because those affected are unable to give such consent, or because dependencies, positions of power and the like effectively mean that informed consent does not afford adequate protection.

7.1.3 The technical function

The technical function can provide clarity and a reliable method of dealing with controversial areas in biotechnology. The legal status of much of what goes on in practice in relation to biotechnology may be unclear in the absence of explicit rules. Regulation can ensure that those involved know what is acceptable or not acceptable so that they can perform their duties and make their decisions in compliance with this.

One example is regulation in relation to scientists performing research involving embryos, and firms working on xenotransplantation, in which those affected by regulation of what is permissible/ not permissible are provided with a legally binding framework such that they do not need to assume any personal responsibility for whether a given research project is to be regarded as ethically defensible. Moreover, rules concerning confidentiality and duty of non-disclosure in relation to genetic information obtained by doctors may also be seen in this context. Furthermore, legislation can guarantee special rights, for example, patient rights, the doctor's right of refusal, the patient's right of refusal and so forth.

Overall, one conclusion might be that the technical function is there to prescribe definitive rules for what is ethically acceptable/unacceptable, and to define precisely which rights and obligations must be observed by all parties concerned - in their mutual dealings and in relation to society.

7.2 Different types of regulatory instruments

Surveying biolaw across Europe, examples of different legislative instruments would include those listed below.

Framework legislation enables the establishment of special forums with the right and duty to undertake evaluation of ethical implications of selected fields in biotechnology. Examples include the appointment of ethical councils, committees for scientific ethical evaluation, bodies imbued with the right and duty to award licences under certain terms, authorisation procedures and so forth. This form of instrument ensures, through parliamentary channels, that a domain may be established in which ethical debate can thrive.

Informed consent has come to represent one of the keystones of health legislation in recent years. Informed consent is consequently a precondition for treatment, medically assisted procreation, participation in clinical trials, transplantation, etc. Rules concerning informed consent serve to guarantee autonomy. Obviously, special problems may arise in relation to children and other persons unable to give informed consent.

Directives, authorisation requirements or the like permit the formulation of provisions that certain treatments, research activities, etc. may be carried out only on condition that a licence, authorisation, permit or similar has been obtained. In addition to which there are the directives prohibiting certain methods, objectives, etc.

Rights may be granted by legislation. One example would be patent protection, according to which a patent holder is accorded the sole right for twenty years to industrial use of a patented invention. Another example would be the right to retain frozen sperm, eggs or embryos following the death of the donor, or the right of relatives to consent to or not give consent to organ donation. A third example would be revocation of donor anonymity such that a child produced by donation is accorded

the right to be informed of the donor's identity.

Prohibition and sanction are familiar forms of regulation. Examples of prohibition and punitive provisions would include bans on cloning, on gene therapy on germ line cells, on "chimeras", etc. and on retaining embryos in vivo for research purposes for more than fourteen days. Other examples would include prohibitions against requiring genetic testing in connection with employment or insurance.

Moratoriums are a form of regulation that have acquired status in relation to biotechnology. Moratoriums suspend activity, giving pause for thought so that the actors involved can find their "ethical feet", and avoid a situation in which it becomes impossible to impose meaningful restrictions because a given practice has become commonplace before it has undergone ethical evaluation. At the same time the burden of evidence is, as it were, shifted, in the sense that those seeking to introduce new practices are obliged to argue their case.

Professional standards can take the form of soft law, that is, guidelines that are not binding in an official, legal sense. Recommended guidelines of this nature may be laid down by a scientific association, and any sanctions for non-compliance with the guidelines may vary. A notable example is the World Medical Association's Declaration of Helsinki on medical research involving human subjects.

Case law, consisting of the written opinions of judges giving the verdict in a particular case, is the standard form of regulation in a number of common-law countries such as Great Britain. According to this system, the link between ethics and law is created by case-by-case verdicts brought before the judiciary. From the specifics of case law, more general ethical principles with legal force can sometimes be elicited.

Regulation of education and research are important models for ensuring the operationalisation of ethical principles. This can be a means of creating scope and tradition for incorporating ethical reflections and considerations at the earliest possible stage in any proceedings. The need to include bioethics as a subject in education comprises both ethical issues associated with a particular field of research or practice, and more general ethical issues. The connection between natural sciences/health sciences, ethics/philosophy and law/social sciences,

ces means that there is a need for an interdisciplinary approach to the issues raised by the new biotechnologies. This can promote direct dialogue and thereby mutual inspiration. It is essential that students be introduced to bioethical issues early on in their studies. At a later stage, bioethical topics can then be explored in greater depth as required, especially in relation to more narrowly defined, subject-specific issues and concerns regarding research ethics.

One noteworthy example of a drive to ally research interests with ethics, environment and safety is found in article 1 of the Norwegian act on genetic engineering, which lays down three general requirements regarding the production and use of genetic engineering, and regarding applied or commercial research: It must 1) be ethical and socially defensible, 2) be in conformance with the principle of sustainable development, 3) cause no damage to health or the environment.

Besides the need to create a common platform for addressing ethical issues, it is important to create a well-founded basis for discussion and knowledge exchange among students and working scientists, so that they can participate in and influence qualified public debate about the ethical questions linked to these issues. Studies (made in Denmark by Peter Sandøe and Gitte Meyer⁴) have shown that scientists and the public not talking the same language represents a serious barrier to dialogue - there are different conceptual interpretations, in that, for example, scientists use a broad concept of utility and a narrow concept of risk, while the concerns of the population at large are expressed as a broad concept of risk and a narrow one of utility, e.g. for fellow human beings in need in the third world, for the sick, or for nature.

7.3 Advantages and drawbacks of different regulatory models

a. Formal regulation

One advantage of formal legislation is that it can fulfil the functions described above, namely to set standards, protect and regulate.

This ensures that the application of biotechnology is not undertaken without control and governance. One could say that the law is used to delineate which of biotechnology's potential applications are desirable and which are to be

rejected. This can come from an assessment of one or more of the ethical considerations that have arisen. It may be judged that there is insufficient financial or qualitative gain - e.g. on the grounds of risk assessments - for a given technology to be applied in a particular way, or it is considered to be contrary to considerations of dignity to admit a particular application.

Formal legislation can be essential when consent does not provide adequate protection, e.g. because the implicated parties' circumstances are not equal, or because a vulnerable individual is involved. Moreover, formal legislation can be necessary where fundamental values are at stake, e.g. regard for future generations, for the environment and so on - where the individual may not perhaps feel responsible in the same way and where the need for a general ruling is therefore imperative.

Legislation can play an especially significant role by emphasising the protective function. Finally, formal legislation ensures that the process is open and democratic.

A drawback of formal legislation is that it is difficult to be sufficiently precise as concerns ethical principles. If it becomes too vague, regulation will fail to provide meaningful protection. If it becomes too heavy-handed, it can risk obstructing progress that is desirable, e.g. by restricting research in an unintended fashion.

Moreover, it can appear as hostile among affected parties, such as researchers and business people, which can be detrimental. Finally, legislation can strip from affected parties their individual or professional responsibility and also in this way be detrimental. And the law does not necessarily render the affected parties ethical.

b. Framework legislation

The *advantage* of framework legislation is that it indicates the specific forums - and hence actors - who have a particular duty to participate in the ethical debate and decision-making process. At the same time, pronounced flexibility is achieved, since it is up to these different bodies to determine how a given task is to be performed in detail and when, for example, an

approval, a licence or similar is to be granted, and when refused.

The *drawback* can be that it may be difficult for the bodies in question to know which criteria to

⁴ Peter Sandøe and Gitte Meyer: Project report: "Oplysning og dialog om bioteknologi i forhold til planter" [Information and Dialogue concerning Biotechnology in relation to Plants], supplement to the newsletter "Bioteknologi i Praksis" [Biotechnology in Practice], Centre for Bioethics and Risk Evaluation, June 2001.

give detailed emphasis to when making an assessment for a licence, an approval or similar. It is therefore important for such criteria to be debated and drawn up - although not necessarily in great detail.

c. Rules regarding consent

The **advantage** of rules regarding consent is that decisive emphasis is given to autonomy. This is appropriate where there is parity between the consent giver and the consent receiver. Moreover there is an assumption that there is a coincidence of interest between the person consenting and anyone consenting on their behalf. Finally, it is important that the affected parties are those embraced by the consent. However, consent is an *inappropriate* or *inadequate* form of regulation in situations where no parity exists between whoever is to give consent and whoever is asking for it. This will at times be the case, e.g. in relation to employee/employer, insured/insurer, etc. Moreover, consent can be problematical where a schism arises between, for example, allowing the mother alone or both the future parents to give consent to research on embryos. Finally, as a form of regulation consent assumes that there is no regard for persons or interests beyond the parties to the consent, e.g. future generations, sustainability, the vulnerability of the natural world and so on.

d. Prohibition and sanction

The **advantage** of prohibition is that no issues are allowed to evade social control, out of the general principle that what is not prohibited is normally permitted. This presupposes precision in the drawing up of regulations.

The *drawback* of prohibition can be that it appears to yield a prohibitive legal position when compared to the needs and benefits that arise in practice. It can be difficult to ensure the flexibility which the dynamic development of the biotechnology area can be said to create a need for. One example is the prohibition on cloning techniques, which may prove to impose tight restrictions on any subsequent intentions concerning stem-cell research, to the extent that these require the use of cloning techniques.

e. Professional standards

Professional standards have the **advantage** that they are agreed upon, and that they therefore may be assumed to arise from internal dialogue and consensus, which means that the affected parties feel duty-bound to abide by the agreed standards, even if they are not binding

- and, perhaps, abide not only by their letter, but also by their spirit. At the same time, they can be easier to amend than formal regulation and so be more suited to the dynamic biotechnology area in a number of cases. They can in this way have a significant conduct-regulating function.

The *drawback* is that they do not include a broader ethical perspective, e.g. not necessarily all questions relating to just distribution of benefits and burdens, vulnerability and dignity, etc. The specialist point of view may often be expected to narrow the aspect of the values and interests involved, since there is not, within professional standards, the same tradition for taking account of wider concerns of protection. The specialist professional standards are centred chiefly on the traditional scientific need for quality - and frequently on the need for consent, regard for integrity, etc.

One particular *development* from soft to hard law can occur, in that a regulation which starts out as "soft law" can become a "locomotive" for a development towards a more detailed legal regulation of an area, and thereby also for establishing binding legal rights for an area not previously characterised by legislative codification. This was the case, for example, with the Declaration of Helsinki, which set forth the first guidelines for the conduct of biomedical trials on humans. This started out as a voluntary professional code, but subsequently created the background and learning environment for much of the development which biomedical research and the treatment of patients has undergone over the past 30-40 years. In Denmark, for example, the scientific ethical committees' work was established by law a decade ago, and this will also happen in other countries as a consequence of the directive on good clinical practice.

f. Case law

A clarification of the legal position by judges has the advantage that a position is only taken when a matter has evolved into a problem, and that a position is taken only on precisely that problem.

The *drawbacks*, however, are obvious. Case law, where the legal development is laid down by judges in the form of a "patchwork" made up of isolated cases, does not generally appear to be especially suited to biotechnology. Firstly, there will be uncertainty as regards what is acceptable or unacceptable until the judgement is made, and that can take a long time.

Secondly, it will be about a specific case, in which only a small facet of biotechnology becomes the object of legal clarification. Thirdly, it will often be a question of a *post factum* ruling, since the applications will be able to continue while the cases are pending. Finally, economic circumstances and, for example, questions about who has the right to prosecute, will lead to positions not being taken on the urgent questions that biotechnology raises.

8 The toolbox

- check-list

The tools consist of two essentially different instruments, which are here termed regulatory models and debate models, respectively. The following sketches out an abbreviated check-list, which can form the background for decisions on the application of the different tools as concerns operationalisation of the ethical principles.

8.1 Regulatory models

Toolbox

Regulatory models

- International conventions, directives
- National legislation of a substantive nature, including prohibition, orders, rights, etc.
- Framework legislation to ensure authorisation procedures, etc.
- Case law
- Professional standards, etc.
- Provisions or practice concerning education, information, debate and dialogue

8.1.1 Choice of forum

- a. Is non-regulation (*laissez-faire*) appropriate for the area, since supply and demand will provide good support and control via the usual market mechanisms, or
 - will the disadvantaged or vulnerable be left in the lurch?
 - will control by the market be too simplistic?
 - will non-regulation disregard groups which cannot speak for themselves, including future generations?
- b. Are professional standards appropriate, since there is agreement in the relevant group and the opportunity for sufficient development of broad and dynamic ethical standards, or
 - will it become more a question of a narrow, specialist point of view?
 - will regulation become too expert-oriented and without appreciation of the population's attitudes and the political level?
 - will the ethical point of view become too narrow?
- c. Is national regulation appropriate, since it ensures democratic control and (reinforced) normative provisions and protection, or

- will the resulting state of law become too inflexible?
- will it be too difficult to amend?
- will it impede progress?

Or is formal regulation necessary to

- protect future generations and culture?
- ensure justice and balance interests?
- ensure that the Community's (societal) interests prevail over individual demands?
- guarantee individuals' rights (autonomy, non-discrimination etc.)?

- d. Is international regulation appropriate, since ethical problems are international and protection is therefore better and equality is increased, or
 - will it result in governance by the lowest common denominator?
 - will decisions be too vague and imprecise?
 - will protection be too weak?

In choosing a forum, account must obviously be taken of what is possible, including consideration of the difficulties of, for example, amending conventions, regulations, directives, etc. At the same time, the choice of forum must take account of whether the individual country has a tradition of formal regulation or common law. Finally, it will be crucial for the regulation to offer suitable guidelines on the content of the ethical assessment. Here, the type of regulation chosen will be decisive.

8.1.2 Choice of type

- a. Precautionary measures, which prescribe specific conduct?
 - might be, for example, a prohibition, an order or a licence.
- b. Prohibition model
 - prohibits some specific research, objective, conduct or similar.
- c. Authorisation model
 - possibly with built-in monitoring and inspection.
- d. Rights model
 - can create clarity
 - can be difficult to manage and sanction.
- e. Discretionary model
 - can accommodate adjustment in line with new knowledge, methods, etc.
 - many different concerns can be incorporated and balanced

- important to define and limit what is to be included in a discretionary consideration
 - openness to interpretation may result in weak protection
 - can be difficult to sanction
- f. Revision model
- frequent assessments as to whether adjustments are required
 - can involve uncertainty
 - in practice, can be difficult to carry out even essential revisions.
- g. Moratorium
- provides scope for an ethical pause for thought, without developments continuing unhindered
 - can halt desirable development in a field
- h. Education
- can ensure that ethical assessments are inculcated in researchers
 - can ensure that ethical assessments become a natural part of the next generation's frame of reference.

8.2 Debate models

Toolbox

- Ethical committees
- Ethical councils
- Technology councils
- Consensus conferences
- Future studies panels
- Values workshops

Use of this toolbox is an extension of the EU Commission's recommendation that societal dialogue and monitoring are important factors, which should accompany and direct the development of biotechnology. The platforms and the ethical debate are comparable with the classical *agora*, in which researchers, legislators, administrators, tradespeople and lay people were convened. As emphasised by the EU in its policy paper, public debate on biotechnology among researchers, industry and civil society should be stimulated, and it is important here that developers and marketers of products assume a distinct ethical responsibility for clarifying potential drawbacks and risks which may occur in relation to the development and utilisation of these products.

Ethical Councils

- ensure that competent individuals feel duty-bound to engage in the debate
- can act as advisors to decision-makers
- the question of membership must be carefully considered, including interdisciplinarity, lay representation, parliamentary representation, etc.
- the question of *modus operandi*, including working groups, expert involvement, etc. must be considered
- How far one should go to achieve consensus must be carefully weighed against the desire to emphasise the nature and value of the arguments.

8.2.1 Consensus conferences etc.

- consensus conferences, future studies workshops and similar can ensure breadth in the public debate
- can be inventive with regard to how the debate is implemented and "staged"
- can provide a pointer as to "public opinion"
- the media can contribute to extending the debate
- narrative writing competitions, essay competitions in schools, videos, etc. can be used to promote participation by the up and coming generation.

PART FOUR

ETHICAL PRINCIPLES IN EUROPEAN REGULATION

- Conclusions and recommendations
- Prospects and challenges
- Postscript

9 Conclusions and recommendations

9.1 Introduction

Biotechnology has much to offer, and much hope is pinned on its potential. However, at the same time, the current and future applications of biotechnology are cause for concern to the extent that large groups of the general public reject certain aspects of it - even where no evidence has been found of any direct, substantive risk.

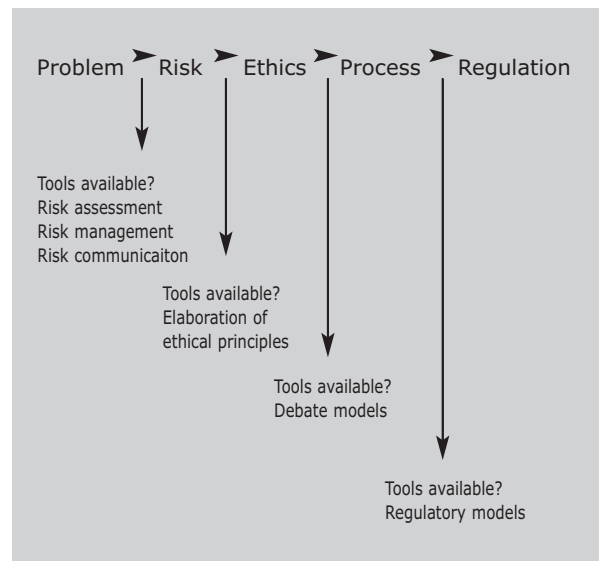
Ethics verbalises the values and the concerns - although it necessarily draws on "yesterday's words" to convey "tomorrow's concerns". In this report the main emphasis is given to the following four "sets" of ethical principles:

- Economic and qualitative benefits
- Autonomy, dignity, integrity and vulnerability
- Just distribution of benefits and burdens
- Co-determination and openness

Firstly, we address the question of how experience accumulated in the area of human health (the "human area") may be applied to the foods area as regards the incorporation of ethical principles in food control. A large body of experience has gradually been amassed in this area, and it would seem pertinent to seek to apply these findings to the foods area; the challenge being to determine whether ethical principles should be incorporated more explicitly in regulation.

Secondly, we consider the question of what barriers and opportunities exist for further operationalisation of these ethical principles in regulating both the human health area and the foods area. To that end, we propose a number of tools that may be employed, while we also present an analysis of what role the individual actors in these areas might play as regards further incorporation of ethical principles in decision-making processes and regulation.

"The Ethical Process" as a concept, and the associated tools available may be illustrated by the following model:



9.2 Can experience from the human area be applied to the foods area?

The following section highlights protection issues, the risk assessments and the ethical principles that have prevailed respectively in the health sector and the foods area, and examines the extent to which principles and findings from the health sector might be applied in the foods area. This is a key issue in the light of the trend in food and product regulation whereby scientific risk assessment is made the arbiter of whether marketing authorisations etc. are granted, while in the health area the tradition has to a far greater degree evolved so as to incorporate ethical evaluation.

a. Protection issues and ethical principles in the health sector

Over the last fifteen years the public health system in a number of countries has gradually distilled off a number of issues concerning the protection of patients receiving treatment from the public health system, and serving as research subjects in biomedical trials. These principles have been expressed formally in documents such as the Council of Europe's Convention on Human Rights and Biomedicine; in the EU's GCP Directive and in a large number of laws in the Member States.

The ethical principle associated with economic and qualitative benefits appears to have been perceived as largely self-evident as it applies to the health sector in the sense that health, medical treatment and, by extension, medical research, are regarded as qualitative benefits. Examples of direct incorporation of the principle are found in the requirement that there must

be “justification” for biomedical trials involving human subjects, and in the Convention on Human Rights and Biomedicine’s affirmation that progress should be for the benefit of present and future generations, and the principle expressed in both this convention and in the Unesco Declaration and according to which the interests of the human being are to “prevail over the sole interest of society or science”. The qualitative benefits in the sense of “protection from risk” are assured through rules concerning prior approval of biomedical research projects, concerning “good clinical practice”, and concerning the responsibility of doctors for medical treatment.

The protection issues that characterise protection of patients especially are autonomy, dignity, integrity and vulnerability. This is illustrated by the principle that medical treatment must not be given without the patient’s informed consent. This also means that medical doctors and other health professionals have a duty to inform patients of any undesirable effects associated with a treatment, and to inform them of alternatives to the therapy proposed. The individual is also entitled to choose to be informed of his/her health condition or to refrain from receiving such information (the “right not to know”). Moreover, health legislation comprises a number of provisions for protection of especially vulnerable groups such as the elderly, children and individuals incapable of giving informed consent to medical treatment. Protection of integrity is ensured through rules governing confidentiality in the doctor-patient relationship, including the doctor’s duty of non disclosure, together with the sanctity of private life, including the right to protection against personal health data being made public, and rules concerning non disclosure of personal data relating to medical information. Human dignity is also emphasised in the Convention on Human Rights and Biomedicine.

Just distribution of benefits and burdens is a principle implemented primarily at the international level. The Convention on Human Rights and Biomedicine, for example, emphasises equal access to health services, while the Unesco Declaration asserts that the benefits of the technologies employed must be made available to all.

Co-determination and openness are emphasised as highly important principles by the EU, the Council of Europe and via a large number of national measures (see Chapter 7 for further discussion).

The principal characteristic of the rules applying in the health area, and that protect patients and research subjects is primarily the protection of all persons, i.e. a highly individual-oriented protection issue. Other ethical principles than respect for the rights of the individual are found in regulations on artificial insemination, which in certain countries entail considerations beyond traditional health issues. Restrictions applying to the individual informed by social and religious values are expressed as restrictions on who is entitled to receive artificial insemination so that, for example, doctors are not permitted to artificially inseminate lesbian women, or as prohibitions against the donation of eggs and/or embryos.

b. The foods area - substantial equivalence - the precautionary principle - sustainability

In the foods area, the basic premise is to employ the scientific principles that have been elaborated and refined over the years. The following section describes the progression in this area from the principle of substantial equivalence towards, on the one hand, the precautionary principle, which has informed international regulatory efforts over the last few decades, and on the other hand, the principle of sustainability, and for each of these principles discusses the possibility of transcending purely scientific considerations to incorporate ethical principles.

The principle of substantial equivalence⁵ was first described by WHO and the OECD in special reference to foods derived by modern biotechnology. According to the OECD definition, existing whole foods may be used as a basis for comparison when assessing the safety of novel or modified foods. If the novel food is found to be comparable with its traditional counterpart in toxicological and nutrient testing, it may be treated in the same way as that counterpart in respect of its safety. Official safety assessments take account of whether proteins are formed that might give rise to allergic reactions, and of deviations in constituent protein, fat, vitamins,

⁵ Source: 97/618/EC: Commission Recommendation of 29 July 1997 concerning the scientific aspects and the presentation of information necessary to support applications for the placing on the market of novel foods and novel food ingredients and the preparation of initial assessment reports under Regulation (EC) No 258/97 of the European Parliament and of the Council (Text with EEA relevance)
Official Journal L 253, 16/09/1997 P. 0001 - 0036.

etc. With regard to deviations as compared with traditional counterparts, novel foods must be assessed on the basis of their unique constituents and properties. Equating foods in this way lends consistency to safety assessments of GMO-based foods versus non-GMO-based foods, but constitutes neither a safety assessment nor a foods assessment *per se*. As such, the principle lends itself purely to scientific risk assessment, and admits no ethical concerns.

The precautionary principle has found favour as a new principle in international legislation. This has happened after GMO-based products in many parts of the world have been met with growing resistance, and doubts as to whether or not they might result in serious, widespread and irreversible damage have been mounting. The precautionary principle is gaining ground in spite of the fact that EU legislation operates with no explicit definition of what the principle actually embodies. In a communication from 2000, the European Commission 2000⁶ offers its recommendations for how the principle should be interpreted within the EU: *"In order to protect the environment, the precautionary approach shall be widely applied by States according to their capacity. Where there are threats of serious or irreversible damage lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation."*

The salient issue here is that the precautionary principle can be applied in cases where the scientific evidence is insufficient or uncertain, and preliminary scientific assessment indicates that there is reason to assume that the degree of risk to the environment and human, animal and plant health would be in conflict with the high standard of protection prescribed by the EU. Application of the precautionary principle also requires that the burden of proof be shifted. Hence it is no longer the authorities or the public sector that has to provide proof of harmful impacts, but rather the applicant seeking to place GMO-based foods on the market, for example. The principle also requires that a given application be reasonably certain and that no preferable alternatives exist. Finally, the principle emphasises the necessity of open, democratic decision-making processes. The precautionary principle thus permits rejection when insufficient scientific certainty exists to vouchsafe the safety of the product. However, it is far from given that the precau-

nary principle would cover a situation in which there were no question of scientific uncertainty, but rather a move to reject a product on other (ethical) grounds. If we consider a parallel situation in human health - human cloning - it is then possible to take into account the view that has dominated the debate (certainly in the Western World), this being "this is unacceptable under any circumstances". This attitude is informed by an altogether different premise from that of scientific risk assessment. But it does not sort as readily under the precautionary principle when referring to GMO-based products.

The principle of sustainability rests on the precept that sustainability must be assured with respect to use of natural resources, to environmental issues and so forth. The definition permits ethical evaluation, but has not by tradition been applied with a focus on the ethical slant of the principle of sustainability. The move away from the principle of substantial equivalence, the precept of which is presumptive ("If it looks familiar, then that's good enough") through the precautionary principle ("If it doesn't look familiar, and might involve a risk to human health and the environment, then we need proof that it's not damaging before we can say it is good enough"), to the principle of sustainability ("If sustainability is at risk, then it has to be rejected") represents a progression from narrow to broad risk assessment. This shift consequently affords us more scope in determining where the risks lie, how they are to be measured and who has to prove what. But these principles would all appear to be evolving out of a scientific premise. The question remains "Is it safe for humankind and nature?", but there is no room for the question "Is it *right* for humankind and nature?".

The precautionary principle and the principle of sustainability allow only limited scope for ethical considerations that are not based on scientific rationale, i.e. in relation to medicinal products, and to a limited extent to the Directive on Deliberate Release, but not in relation to concrete ethical provisions concerning authorisations for placing such products on the market. The reason that the named principles have taken on this format and sphere of application presumably derives from the fact that they concern products that are differently and more immediately bound up with free mobility, the wish for non-discrimination, etc. - these being

⁶ Com (2000) 1 "Communication from the Commission on the precautionary principle". The communication states that the precautionary principle was laid down in the Rio Declaration of 1992, in which the quotation appears from Article 15.

key issues for both the EU and the WTO. Consequently, for GMO-based foods, the tendency has been to allow decisions concerning marketing authorisations in the EU to be based solely on scientific risk assessments.

This begs the question of whether scientific principles should not be complemented by a "principle of ethical precaution" in evaluations of the extent to which research should be undertaken on a particular product, or whether marketing authorisation should be granted.

9.3 Ethical principles in the foods area?

As highlighted in the section on risk assessment, biotechnology raises issues concerning both risks and values, and scientific risk assessments alone cannot embrace the scope of the value-based issues underlying the entire GMO debate. There is no sharp divide between scientific risk assessments and political risk management; risk management is not a well-structured balancing of costs and benefits, and risk communication does not address the dilemma between the actual (objective) risk and the perceived (subjective) risk in which knowledge and values are commingled.

It is our position that the key aim in this context is to link up all the elements of scientific risk assessment and political risk management and the dialogue on risk management to ethical considerations and evaluations.

Two examples will serve to illustrate the problem, and the difference between scientific risk assessments and values-based, ethical assessments:

In recent years the debate on BSE has indicated clearly that it is not merely a matter of scientific risk assessment that determines whether or not the public can accept exposure to a risk. And yet the risk of contracting BSE by eating beef proved slight, and for the experts the force of public reaction was something of a mystery. The reason for the force of the reaction against this particular risk may possibly be traced back to the fact that people felt that behind it all, certain ethical principles had been violated, when it emerged that the disease was thought to have arisen when cattle were fed on feed enriched with bone-meal, that is, feed containing residues from animal cadavers.

Many presumably felt that it was "unnatural and against nature" to feed cattle with animal-based feed, given that cattle are herbivores. In this context it is important to recognise that in

the public's perception of their willingness to accept exposure to risk a number of ethical issues and concerns are also involved, which may not necessarily be expressed as such, but that nevertheless strongly influence public opinion. This meant that while the arguments were based on scientific risk assessment, the reactions were conceivably based on ethical evaluations.

To take a hypothetical scenario: if we were to arrive in a situation where an initiative was proposed in the foods area along the lines of the example of human cloning, the problem might occur in a pure form. If, for example, it proved cost-efficient and safe (by scientific standards) to produce meat by culturing human muscle tissue outside the body using genetic engineering, then the scientific principles would not necessarily ensure that such a product would be the object of ethical deliberations. Indeed, access to a cheap and perhaps very healthy and nutritious source of protein might conceivably be justified by socio-economic interests in access to affordable protein for poverty-stricken populations. Nonetheless we can readily conjecture that there would be a lack of acceptance of a food of this nature based on ethical evaluations - in line with public rejection of cloning (and possibly drawing on parallels with cannibalism).

The need to be able to make ethical evaluations with respect to food products also would thus appear to be present. An important objective for democratic and dialogue-oriented risk management and risk communication must be to open up the parameters for legitimate objections that would also comprise wider ethical issues. Against this background it is useful to examine the four ethical principles addressed in this report, and to explore whether there is justification in the foods area as regards product marketing to address the same protection issues as those involved in human health concerns.

The ethical principle associated with *economic and qualitative benefits* has a more restricted role with respect to the marketing of products in the foods sector than it has in the health sector. Genetically modified foods are scarcely perceived as a qualitative benefit comparable with the offerings of the health sector, including medicinal products. One interesting idea would be an ethical assessment of whether there was "justification" for research, deliberate release or product marketing on the basis of an assess-

ment of economic and qualitative benefit. In that context it would presumably be most realistic to apply any ethical considerations at an early stage rather than at the product marketing stage. One aspect that also arises in this context is the environmental issue and thereby also concern for future generations. Here it is important to consider which decisions would be irreversible.

Autonomy, dignity, integrity, and vulnerability do not amount to the same central issue in the foods area as they do in the health area. The vulnerability of nature is an element in protection of the environment and biodiversity, while dignity, integrity and vulnerability are principally associated with the human area in that they concern protection of the human being. The principle of autonomy, however, can be readily applied to the foods and product area. The principle of free information and the individual's freedom of choice might suggest a principle of autonomy with regard to whether or not the individual wishes to consume genetically modified foods. This would then entail a need for measures to ensure that labelling at every stage in the food processing chain clearly indicated genetically modified content. However, it is arguable whether labelling of this nature designed to observe the need for autonomy should be required in instances of significant GMO content, or in all instances.

Just distribution of benefits and burdens is a principle found primarily at the international level. The Unesco Declaration, for example, stresses that the benefits of work on the human genome must be made available to all. In this context it is important to be aware that while ethical evaluation might result in restrictions on GM foods, they might conversely result in measures to promote them in so far as they improve the capacity to feed people in the developing countries, for example. The principle is also expressed in the principle of sustainability and the Convention on Human Rights and Biomedicine.

Openness and co-determination are emphasised as key principles by the EU, the Council of Europe, the Aarhus convention on the environment and a large number of national initiatives (see Chapter 5 for a more detailed discussion). In that context it is important to be aware of at least three factors. Firstly, that the ethical process seeks consensus, but if this is regarded as unattainable the process will aim for "fair play despite differences". Secondly, it is important to

respect arguments based on wisdom on an equal footing with those informed by a scientific rationale, and to acknowledge that ethical arguments can be just as valid as economic arguments. Thirdly, it is important to prescribe regulation and practice in such a way that they respect the individual consumer's autonomy and freedom of choice so as to prevent ethical "vote-down" of minority views on issues where no positions aimed at the common good and no concern for future generations necessitate a common position in violation of the individual's freedom of choice. To that end, regard for Europe's new multicultural societies might support a move to create regulatory scope for differentiated freedoms of choice that do not conflict with concern for the common good. It is important to link ethical principles up with dialogue between those directly affected and the state, in order to arrive at a viable decision-making process on the use of novel biotechnology in the foods area.

9.4 How are ethical principles operationalised in regulations?

Any detailed discussion of how ethical principles may be incorporated and operationalised in decision-making processes and regulation presupposes that the component barriers, assumptions and possibilities have been crystallised out, and that a number of central questions have been settled concerning political will, scope, actors, timing and choice of tools. But by way of introduction we can now summarise which ethical principles and regulatory challenges are involved:

9.4.1 Regulatory challenges and possible tools

The object is to ensure that certainly the four fundamental ethical principles discussed in the foregoing of benefits, autonomy, just distribution and co-determination are incorporated in regulation of biotechnology.

International *regulation* is characterised by two different trends:

Firstly, there are a number of international conventions, declarations, etc. that emphasise very broad, general ethical principles. This applies to the human area, e.g. the Unesco Universal Declaration on the Human Genome and Human Rights, the Council of Europe's Convention on Human Rights and Biomedicine and the EU Charter of Fundamental Rights from 2000. Rights in this context are centred especially on the ethical principle associated with autonomy, dignity and integrity, and to some

extent the just distribution of benefits and burdens. In the environmental and foods area ethical principles do not apply in a narrow sense, but rather to general principles of "the right to the environment", the precautionary principle and the principle of sustainability. However, to some extent the ethical principle discussed in the foregoing, of openness and co-determination, comes into force in, for example, judicial rules concerning hearings.

Secondly, there are the precise provisions, directives, etc. in the EU domain governing a number of issues. This applies to the EU directive on clinical trials on medicinal products for human use. However, it applies especially to EU provisions and directives concerning foods, which by means of comprehensive and complex authorisation schemes enforce risk assessment for health and the environment, and the labelling of GM foods.

National regulation is particularly relevant in the human area, especially in connection with medical treatment, since the foods area is largely covered by EU controls - usually in the form of total harmonisation. In the human area regulation varies considerably when it comes to intensity, content and format, though there still a number of areas that have resulted in national regulation, e.g. artificial fertilisation, genetic testing and gene therapy, cloning and (future) biobanks. In this way the ethical principles concerning autonomy, dignity, integrity, etc. are often covered. In addition there is the regulation that creates the framework for ethics committees and the like, the purpose of which is to secure information and debate on ethical issues relating to biotechnology in one form or another and/or which have a specific mandate to grant authorisations for certain applications of biotechnology.

In the health area there is thus extensive scope for incorporating ethical principles in decision-making processes and regulation. In the foods area the scope of individual nations for incorporating ethical principles is, however, limited when it comes to product marketing as a result of the goal of total harmonisation based on rules that do not give scope for ethical considerations. The foods area is extensively covered by WTO rules, which give precedence to the principle of free trade, and thereby focus more on eliminating barriers to trade than promoting ethical concerns. Nonetheless, WTO agreements and rulings reveal that other concerns do find favour - for example, the concern regarding exhaustible natural resources and

public order enabling consideration of "public order and morality". It is hence worth considering to what extent these new trends may be employed in introducing ethical considerations when these have sufficient primacy and importance.

This report presents a whole series of tools that can be used in operationalising ethical principles. These are divided up into the so-called "debate models" and "regulation models", and the report highlights a number of the benefits and drawbacks of the individual models.

The debate models consist of

Toolbox

Debate models

- Ethical committees
- Ethical councils
- Technology councils
- Consensus conferences
- Future studies panels
- Values workshops

The regulation models consist of

Toolbox

Regulatory models

- International conventions, directives
- National legislation of a substantive nature, including prohibition, orders, rights, etc.
- Framework legislation to ensure authorisation procedures, etc.
- Case law
- Professional standards, etc.
- Provisions or practice concerning education, information, debate and dialogue

A checklist is provided for the purpose of highlighting a number of factors that in any event should be addressed in considering the applicability of the various models.

9.4.2 Political will and regulatory scope

If there is to be greater operationalisation of ethical principles in regulation than happens currently, it is essential that the political will is present to realise this aim. This applies at national level to parliaments, governments, authorities, etc. It also applies at international level to international forums of various kinds. Under EU auspices it is especially important

that a political commitment is expressed by the European Parliament and the Council of Ministers to greater operationalisation of ethical principles in regulations, and that this is supported and implemented by the European Commission. In that context it is significant that the EU Commission in its communication *Life Sciences and Biotechnology - A strategy for Europe*, which was ratified by the EU Council of Ministers, chose to emphasise that the life sciences and biotechnology should be developed in conformance with ethical values and social objectives.

The Commission also emphasises the importance of promoting information and dialogue with a view to giving the public and affected parties a better means of understanding and assessing the complex issues associated with the application of biotechnology and of developing criteria, including ethical guidelines/norms and methods for weighing up the benefits against the drawbacks and risks. Exactly how operationalisation on these lines might be brought about will depend on what options and restrictions present regulation comprises.

The restrictions against incorporating ethical principles in regulation currently derive from statutory instruments, directives, etc. according to which total harmonisation is achieved for an entire area. This applies to a proportion of EU regulation in the foods area, for example, which means that it is not possible to incorporate and operationalise ethical principles without amendment of these rules or the introduction by some other means of, e.g. the ethical principle of co-determination and openness.

It is therefore important that this type of regulation is elaborated in such a way that it gives scope for ethical considerations. Examples of an opening up for the possibility of incorporating ethical considerations exist in the patents directive and the directive on deliberate release. These directives open up for the possibility of consulting the EGE (European Group on Ethics in Science and New Technologies) on principal ethical concerns raised by the directives. However, the difficulty lies in establishing exactly what the ethical principles cover, how they should be interpreted and how they should be incorporated in the processing of actual applications.

9.4.3 Actors: role and scope of action

In connection with operationalisation of the ethical principles it is essential to carry out an

analysis of actors in order to ensure that the right ones are involved, and to consider how the actors themselves can further promote the application of ethical principles.

Actors

Who are the actors?

- Researchers
- Commercial actors
- Affected parties (environmental groups, patient associations, other interest groups)
- Decision-makers (politicians)
- Administrators (public authorities)
- The media and communication
- The general public/lay people

a. Researchers are usually first on the scene. Researchers have an important role to play as regards observation of ethical principles in the sense that they are both the suppliers of specialist knowledge of the research and its possible applications, and the suppliers of research on ethics and on the social impacts of biotechnology. While academics in pure science and the health sciences will often be qualified to comment on aspirations regarding the application of research in industry and in combating disease, other academics, such as sociologists, psychologists will be needed to comment on the consequences for society at large, human interaction, self-perception and so forth. An interdisciplinary approach to the problems is therefore crucial. In this context it is also important for academic institutions to assume a responsibility for generating and supporting the interdisciplinary approach required in addressing biotechnology issues, especially as the initiators of forums for encouraging knowledge exchange among the different disciplines.

Generating knowledge

- Who possesses what type of knowledge?
- Researchers - typically work with baseline **data** and generate **information** from this
- They generate expert knowledge, typically of a technical/scientific nature
- Generated knowledge: expert knowledge - information
- Law, sociology, ethics, philosophy are meta-disciplines that incorporate raw data produced by (pure) science

In operationalising ethical principles the roles of researchers can be developed in various ways.

One approach is for ethics to be incorporated more extensively in the training received by pure scientists so that they may be better qualified to engage in ethical debate, and perhaps also have a greater sense of duty to initiate debate in their particular field of research (see Chapter 8). Furthermore there is a need for greater involvement of researchers in the social sciences and humanities. Finally, it is vital to establish forums, in which researchers can engage in dialogue with counterpart academics and thereby contribute to the factual information generated, while also helping to identify present and future ethical dilemmas in a given issue.

b. Commercial actors and affected parties

will often have a direct and transparent interest in a specific application of biotechnology, e.g. as a patient hoping for a new medical cure or as the manufacturers of GMO-based foods. Moreover, affected parties may include persons and groups with a highly differentiated approach to the problems, e.g. as environmental watchdogs, lobbyists for the precautionary principle, etc.

When it comes to operationalising the ethical principles, the role of commercial actors can be extended by promoting their involvement in forums comparable to those for researchers. This would be valuable for several reasons. Firstly because "the ethical dilemma" might be "bad for business" in the sense that sales may fail if the product in question is regarded as ethically undesirable. Secondly, because commercial actors, like other citizens have a shared responsibility (and often desire) to engage in, and contribute to, ethical debate in their line of business. Other affected parties such as patient associations could be represented in issue-specific ethics committees. Interest groups can be encouraged to participate by means of "the right to know", hearings, representation in ethics committees, the right of complaint, court trials and the like. The model produced by the Norwegian values workshop on the future of the fisheries industry (see Chapter 6) could be held up as inspiration for initiating a sector-wide debate in other countries. On these lines it might be observed that the pharmaceuticals industry is approaching a stage where ethical considerations will be a competitive parameter.

c. Decision-makers are required to draw on facts, evaluations and ethical choices to determine the extent to which, and the manner in which, ethical principles are to be observed. For

these actors, tools are crucial.

In places where no ethical councils exist, these should ideally be established to undertake informative, debate-promoting and advisory programmes in order to give decision-makers a qualified basis for addressing ethical issues.

The existence of such ethical councils could also be assured by means of legislation.

Furthermore there is of course the key role to be played by decision-makers, that is, initiating the incorporation of ethical principles and considerations in definitive rulings and regulatory processes. This could be in the shape of normative work on ethical components, but often it might also be a pertinent element in regulation of processes, in order to ensure the existence of official bodies and procedures for conducting the actual ethical evaluations. However, to that end it is vital for decision-makers to go one step further and also supervise the elaboration of guidelines by which the ethical principles may be defined and operationalised. One example is the EU directive on good clinical practice and the Danish act on a scientific ethics committee system (see Chapter 4 and Chapter 6), both of which present a detailed check-list for the evaluation to be conducted by scientific ethics committees in vetting proposed research projects.

d. Administrators are mandated to implement the letter and "spirit" of the law in authorisation procedures, etc. This may be straightforward when the criteria are explicit, but the ethical principles will often be relatively vague in the sense that they are open to a wide array of interpretations, ranging from the strictest interpretation of what constitutes a violation of the principles of integrity and vulnerability, for example, to a more lax interpretation. The more accommodating the legal norms are, the greater the decision-making authority will be among administrators. This makes the way in which approval bodies, for example, are appointed and made up all the more decisive.

Knowledge governance

- Administrators - work with information, but rarely do more than simplify and communicate this knowledge - to affected parties (applicants, etc.), politicians and the public
- They do not generate a new type of knowledge, but process expert knowledge.
- Generated knowledge: processed expert knowledge/information

When coordinating process regulation and developing guidelines for decisions on actual applications, administrators, like decision-makers, require ethical information and external evaluations. They may also need more explicit policy-based statements as to which ethical principles are to be incorporated in an administrative regulation; an evaluation of an application and how these are to be weighted in relation to each other.

Ideally, the EU should play an extended role in promoting the interdisciplinary approach in relation to the administrative level also in such a way that ethical issues concerning the human area, animals area, plant area and foods area may be considered and appraised across the board.

e. The media and communication The media have an important role to play in communicating information and as initiators and central co-actors in national debate. They often have a constructive contribution to make to debate, but are not bound by the same obligations concerning balanced and consistent views that are imposed on decision-makers, administrators, etc.

Ideally, the media should also communicate and promote debate on topics that transcend sensationalism or "war" between conflicting interests to contribute to a more nuanced debate.

When it comes to communication of risks, it is important to ensure that this is not regarded as a one-way push to convince the public that genetic engineering per se is to the good and a sign of technological progress. The latest Eurobarometer polls of public opinions on biotechnology have also revealed that it is not public's level of understanding of the technologies involved that determines their attitudes to the technology. Instead, risk communication should be a "multi-channel" communication in which several actors join forces and return input to each other. Scientists, decision-makers and administrators will in this way not only be suppliers of output, but also recipients of output from industry, interest groups, lay people, etc.

f. The general public/lay people are important actors as regards the safeguarding and communication of the "wisdom" present among them. The public needs to be consulted, and society as a whole needs the public to contribute with the wisdom it embodies.

Wisdom?

- Wisdom is generated from data - information, but who does this, and who possesses wisdom?
- If scientists and decision-makers process information on the basis of ethical principles, perhaps wisdom can be generated?
- Is it also true to say that wisdom exists in the population, when considering ethical decision-making processes - and that Scandinavia's tradition for using lay people in various organisations, councils and boards may be interpreted as recognition of this wisdom?

It is important that lay opinions are made on a well-informed basis. The foundation for lay opinion might be achieved by: a thorough grounding in the topics to be assessed, including access to expert opinion such as a dedicated secretariat that can provide specialist knowledge geared to lay people so that their opinions may be well-informed and supported by the facts. At the same time it must be ensured that there is scope for lay people to form their opinions without being voted down by formally qualified experts. Here again, the Norwegian model, in which lay people help to define and weigh up a number of ethical principles in an ethical matrix can provide inspiration. Lay people should be included both as participants in public debate and as active members of ethics committees both in consultative forums and on committees set up to vet specific projects.

The domain occupied by the actors addressing the new biotechnology creates a need for a type of forum in which the term agora from ancient Greece can serve as inspiration. This is a form of market place, established by decision-makers with the aim of convening actors (stakeholders) to exchange views with each other and the general public. In ancient Greece this was where public administrators, the judiciary, philosophers and traders assembled to administer, exchange views and do business. At a time where science and its application is a multinational issue that will also have impact on future generations, should be established at local, national and international levels alike.

9.4.4 Debate: polycentrism and timing

As stated, elements from many different discourses and contributions are involved in ethical debate and in the decision-making process concerning regulation.

The generation of a form of ethical consensus is a process akin to theories concerning polycentrism in law. Law is created not only within a single forum, but in many different centres. The formation of laws is therefore not a mono-centric process, but is polycentric in that it goes on in several spheres and is the object of dynamic exchange among different centres and levels. The legal experts Henrik Zahle and Hanne Petersen in Denmark have explored this theory of polycentrism in legal science.

The ethical process is characterised by the same polycentrism. Ethics are no longer formulated by a single proponent (for example the church) but are evolved in an interaction of forums and actors. If a legislator or authority wishes to promote ethical debate it is therefore important to analyse out the actors in order to initiate an ethical debate among their ranks (for example, in the particular sector that will be affected such as the food industry, agriculture or pharmaceutical industry). It is then also important to link up the debate ongoing at the different centres - who will be talking to whom so that we can be sure that an opinion is generated on the issue to be settled? Moreover it is important to sustain debate and dialogue - how do we ensure that debate and dialogue do not peter out - how is momentum sustained?

A polycentric debate should be a phase devoted to settling issues and discussing them and thereby the precursor of a process to arrive at an enhanced regulation strategy based on a clear perspective of the general public's and the actors' attitudes to an issue prior to legislation. The debate phase calls for both an interdisciplinary component and recourse to the wisdom embodied by the general public. In this context the media have an important role to play, and the various forms of debate model can be employed depending on culture, traditions and so forth.

Timing is an element that is essential to stress in connection with ethical debate. The Danish Council of Ethics has adopted the motto "Ethics Just In Time". As the words suggest, this means that ethical debate must not happen too late, but nor must it start too early. If ethical debate comes too late, products will already be

placed on the market, and the risk is that there is no issue left to debate.

If it happens too early the risk is that no one will have any feel for the issues. The questions will not be taken seriously and ethical debate will fall by the wayside. Two examples of this will serve to illustrate the problem:

In the mid-1980s the then Danish Ministry of Health produced a report for the Danish Parliament, Folketinget, on gene therapy.

This was met by deafening silence - simply because the issue had been raised too early.

The same was the case with the debate on Dolly, the first cloned sheep. Everyone claimed that the public was astonished that cloning was even possible, despite the fact that a study of newspaper cuttings revealed that the capability had been reported in newspaper articles for several years previously.

It is thus important to plan the timing of ethical debate and the operationalisation of ethical principles. This should be based on an assessment of when the debate will be sufficiently newsworthy and merited. Perhaps it should be conceded that what is really needed is "Ethics All the Time" - when research is planned, when it is carried out, when its results are studied, and when it is applied.

9.5 A choice of tools

In the following we discuss the tools available in the various areas. It should be strongly emphasised that these are not proposed as definitive and absolute solutions, and are rather suggestions for providing a point of departure for forming opinions. In proposing these as tentative solutions it is in recognition of the fact that it is often more productive to address a concrete issue than to have to begin deliberations "from scratch". The proposed solutions should, however, be adapted to the given situation, culture, tradition, etc.

The following also proposes how the "buffet" of options can be worked into set "menus" comprising "starters", "main courses" and desserts, i.e. debate models, international regulation and national regulations (and professional norms).

9.5.1 The debate models

The "starters" are the debate models. In our opinion these are all-essential both as a democratic component for ensuring openness and co-determination, and for testing out the prospects of achieving acceptance and even consensus on a given issue. It is important to

establish forums from which ethical debate can be initiated. Debate should engage both those directly affected and the general public, who should be assured of the right to information and participation in decision-making (cf. the Aarhus Convention). Both interdisciplinarity and the incorporation of lay wisdom are essential in this context. It is equally important that ethical debate is taken seriously rather than ending up as a "show dish". If the general position is that the application of certain aspects of biotechnology is undesirable then this should be respected. In order to ensure broad debate, formal regulation - national and international - should establish forums in which ethical debate can flourish.

These then are "menus" offering many variations on the "starters", but these must not be omitted, since this would "send the guests home hungry".

9.5.2 National regulation

Besides ensuring ethical debate, proper formal regulation at the national level is especially important when it comes to areas not governed by binding EU regulation, and where the following circumstances obtain:

- a. Where there is a need to protect future generations.
In instances where sustainability is an issue, for example.
- b. Areas where cultural considerations are involved.
Where the issue concerns treatment of embryos for example.
- c. Protection of groups in the population unable to look after their own interests. (vulnerable groups)
Where the issue concerns children, people with mental disorders or senile dementia for example.
- d. Situations in which there is inequity between those affected (dependency).
The issue might be genetic testing in the context of employee/employer or insured/insurer for example.
- e. Cases where competence needs to be ascertained.
Concerning the right to artificial insemination for example.
- f. Areas in which autonomy must be protected.
In questions of rules regarding informed consent or information, for example.

Many of these areas will also be suited to international regulation, but in a number of areas

there will be a distinct difference in how ethical opinion "turns out". A typical example is "the status of the embryo". Generally there may be a difference among nations (national trade-marks) as a result of:

- religion
- state/individual
- national economy/social conditions
- regulatory tradition
- other

It should presumably be accepted that in such cases that it will not possible to reach agreement (as things stand) at the international level, nor within the EU. By achieving the right "timing" the process involving formal regulation will also be able to help to establish the normative function that might promote (wider) acceptance of a specific application of biotechnology. However, this should be achieved without any ethical "vote-down" of minority views. In order to guard against "ethical minimalism" it is essential that such principles are contained in substantive, content-specific regulation. Moreover, it may be expedient to aim for more "process oriented" regulation, for example, in the form of scientifically-based ethical evaluation of specific biotechnological (biomedical) projects. When framework legislation is passed, it is of great importance that relatively detailed and explicit guidelines are provided for which components are to be comprised by ethical evaluation, and according to which principles the concerns are to be weighed up. All too often there is a "quantum leap" between very generally adopted ethical principles and actual position, and guidance on how this leap is to be made should be comprised by motives or administrative guidelines for the evaluation for example.

9.5.3 International regulation

Many components laid down in national regulations will also have relevance for international regulation. In the following we indicate areas that would appear of particular importance and pertinent to take account of in the international domain.

It is essential to establish formal prohibitive regulation or the like under international auspices in areas where there may be a significant risk for the next generation, for example, in relation to:

- the environment
- reproduction (e.g. reproductive cloning)

- irreversible damage
- epidemic impacts (xenotransplantation?).

Besides these, other notable areas in which international regulation might be appropriate would include consumer protection, quality criteria for, e.g. biobank storage and labelling (traceability) of GM foods, for example. Another area undergoing extensive internationalisation is biomedical trials. The pharmaceuticals industry's internationalisation of clinical trials has stepped up the need for universal rules for ensuring sufficient scientifically based ethical scrutiny of trials involving human subjects. Internationalisation calls for international rules, but also for international networks - in the field of scientific ethics there will be a need for networking among the committees set up to address the specific problems associated with scientifically based ethical scrutiny.

A number of the areas discussed in more detail below in the context of national regulation (for example, the protection of employees and the insured) might also benefit from an international format. The issues involve a degree of "Europeanisation" of the ethical questions and answers, which will presumably result in greater consensus over time in the areas discussed.

9.6 Conclusion

The dilemma facing regulatory bodies is often referred to in very negative terms as a choice of either major principles and lofty, vague, concrete rules borne out of consensus, but which out of ignorance of the technologies are condemned to insignificance, or, explicit, precise rules that are restrictive and only prescribe for current issues and are therefore condemned to premature obsolescence.

In our opinion this pessimism is neither helpful nor justified. However, it is true to say that the outcome of research is essentially unpredictable, and that this presents an obstacle to the aim for regulation to draw on predictable values. But by employing models that contain both robust international "brake pads" at the all-essential level, and also flexible regulatory models, such as debate models and national framework legislation, ethical principles can yet be operationalised. This will enable social responsibility to be assumed, which will prevent privatisation of ethical issues and hence ensure that core ethical principles are observed.

If we now turn to some of the EU directives, we find that there are differences in which ethical principles they take into account:

The EU directive on clinical trials on medicinal products for human use require an ethical evaluation to be carried out, and require that this must be performed on the basis of predefined ethical considerations (balancing of benefits and integrity). The directive also meets the requirement for ethical evaluation to be concrete in relation to each individual trial. Against this, the directive does not require the involvement of lay people following an open consultative process. In the latest review of the directive on deliberate release, the preamble states that ethical considerations concerned with approval of the release of GM crops are to be incorporated. However, the directive on deliberate release makes no reference to ethical considerations and does not stipulate the involvement of lay people following an open consultative process.

If we consider the four ethical criteria, we also find significant differences among the regulatory options for translating these into legal requirements.

The criterion of **economic and qualitative benefit** essentially reflects the ethics of utilitarianism. This criterion entails assessment of any potential damage and risks, together with assessment of both economic and qualitative benefits. An assessment of this nature can be expressed relatively simply in regulations, and implemented according to a relatively objectivised process. The fact that the last-named component amounts to an estimate of whether the benefit to be derived from an application of genetic engineering would be greater than any damage or risks is not exclusively a regulatory problem. Estimations and weighing up of "pros and cons" is a common element in much regulatory work. However, one difficulty might be that while a criterion may be already established in the human area, and to some extent also as regards animals (higher living organisms), it may only have gained scant recognition in relation to the food product area, i.e. GM foods and crops. In the last-named area, the regulatory premise traditionally dictated that anything that does not carry an unacceptable risk of damage to human beings or nature may be placed on the market. This presents a fundamental dilemma when it comes to introducing more comprehensive assessments in connection with product authorisations.

The criterion of **integrity/vulnerability** and the criterion of **just distribution** are probably the two criteria that present the greatest regu-

latory challenges. This is primarily due to the fact that these criteria entail broad estimations, which can be difficult to standardise on to ensure that the result of their application meets fundamental requirements for legal protection, i.e. predictability. Conversely, it is generally recognised - at least in relation to certain applications of gene technology - that the ethical considerations involved are of great significance. An obvious example of this is reproductive cloning, which many find should be banned because it is a violation of human integrity. In many other areas, however, there will in all likelihood be great difference in opinion on whether the application of a field of gene technology would be in violation of the integrity criterion. As long as the issue concerns procedural regulation, however, it should in principle be possible to incorporate considerations of this nature also, though as already stated, it will scarcely be feasible to legally verify that such criteria have been met.

The criterion of ***openness and co-determination*** is essentially a procedural requirement that may be identified with relative ease in regulation in the form of requirements regarding administrative routines and decision-maker forums. As regards the technicalities of regulation, the criterion can be translated into a requirement that the decision entailed must be made following the involvement of lay people and in such a way that the decision-making process is conducted in the public domain. Such requirements could be operationalised either at a general level, or in the form of detailed regulation of authorities' decision-making processes, including the detailing of rules on the extent to which lay opinion is to carry binding effect. Standardisation of this criterion may be expressed either as requirements regarding the decision-making processes employed by EU institutions, or as requirements regarding the decision-making processes of national authorities. In the last-named case there will presumably be limits to the detail in which the requirements could be prescribed at the EU level.

Finally it should be emphasised that the four ethical criteria should all be incorporated in any assessment of gene technology applications. The final decision should be made by weighing up the assessment made of each criterion. As such there can be no question of straightforward decision-making requirements according to which just a single criterion or all four criteria must be met, but rather a coherent balancing of one against the other. This presents yet

another problem in standardising on the application of ethical criteria in formal regulation.

Overall, the conclusion has to be that while two of the ethical criteria may be expressed relatively simply in procedural regulation in substantive terms the two others can be expressed only in more general terms in regulation. Some of the ethical criteria thus entail assessments based largely on estimation. Moreover, there is the fact that an overall assessment must be made of all four ethical criteria, which again, will be based largely on estimation.

The next step is to lay down rules for how the final outcome of the overall ethical evaluation should be incorporated in the scientific risk assessment undertaken in parallel with the ethical evaluation. Thus, a decision must be made on how the ethical evaluation and the scientific risk assessment should be weighted against each other in a final, official ruling.

The conclusion is thus that it is feasible from a legal point of view to incorporate ethical criteria in EU regulation of the application of gene technology. This may be achieved by operationalising requirements to that effect in procedural regulations comprised of the following components:

- 1) a requirement regarding ethical evaluation;
- 2) formulated ethical criteria;
- 3) including an open process to ensure co-determination.

Against that, it will be inordinately difficult for regulation to prescribe the significance or impact of ethical evaluation. Nonetheless it is essential to address these aspects, especially the question as to how far ethical evaluation can "displace" scientific risk assessment both in a positive and negative sense. This then opens up for two possible scenarios: A scientific risk assessment reveals that the application of a field of genetic engineering might be attended by a certain degree of risk. If the ethical assessment finds little objection to authorising this application, should it then be allowed to proceed? Conversely we have a scenario in which a scientific risk assessment reveals that there is no attendant risk in application of the field of genetic engineering, while the ethical assessment questions the justification for approving the application. How would this scenario be dealt with?

In considering this dilemma it is important to bear in mind that regulation at the EU level is not driven solely by content-based political assessment, but also by the general aim of ensuring uniform laws and thereby a single market in the EU. This produces two likely consequences. The more that ethical evaluation is performed at EU level, the more it can rest on estimation and still produce uniform laws. The more that ethical assessment is performed at national level, the more can it take into account differences in national culture and values, and the more it can ensure an open process and co-determination.

Consequently our position is that while incorporation of ethical criteria in EU regulation is feasible it is also associated with considerable challenges. Furthermore it may be noted that regulation will to a large extent amount to procedural standardisation, and that the consequences of a decision-making process at the EU or national level will be significant. The essence of the conclusions presented here may also be expressed to say that the incorporation of ethical consideration in EU regulation concern dialogue and decision-making processes just as much as they do the legal technicalities of regulation.

Thus it should be expected that there will be a need for both regulation proper - social ethics from the top down - and acceptance from stakeholders in the broadest sense - i.e. ethics from the bottom up. Top-down and bottom-up will, however, be equally important. Biodiplomacy is one of the new concepts in the area.

10 Prospects and challenges

In the area of human health a number of ethical principles have now been adopted, but often after a quantum leap from general matters of principle to concrete interpretation and evaluation, in which dialogue and debate forums have often been lacking.

There is therefore a need for

- national implementation of international conventions;
- concrete guidance for administrators;
- dialogue forums among the different actors, and
- further scope for public debate.

The tools that serve as aids are the debate models, but discussion of the regulatory models and their application will hopefully also serve as inspiration.

In the foods area it has been more difficult to elaborate ethical principles since the "classical" principles associated with the human area of dignity, integrity and autonomy do not have quite the same meaning in this area. The foods area therefore involves more scientific risk assessments linked in with the precautionary principle and the like. Tentative efforts have been made to get ethical principles associated with co-determination and openness adopted, but at the same time, the quantum leap from scientific risk assessment to ethical evaluation informed by values has as yet not been made in this area, perhaps because it is difficult to get this assimilated in a more market-oriented and product-based area.

There is therefore a need for

- crystallising out ethical values in the foods area;
- incorporating ethical assessments;
- concrete guidance for administrators;
- dialogue forums among different actors, and
- further dialogue and debate.

In this area also the debate models should therefore be expected to have a significant part to play in the future, while the regulatory models especially will be geared to the international level.

One concrete proposal might be a **general framework for operationalisation** of ethical principles at EU level:

a) A joint European Commission and Council of Europe resolution concerning, **which general ethical considerations** should be incorporated in vetting biotechnology applications and the creation of **topical dialogue forums**

b) A joint communication concerning "good governance" in respect of decisions/rulings on the application of biotechnology - with elements such as scientific risk assessment, incorporation of ethical considerations, openness, information and debate, the use of ethics councils along with lay participation, etc.

It is difficult to prescribe formulae for ethics that will allow them to be operationalised - but it is important to do so - if necessary by practising on different models.

And it is better to sample the entire "menu" than "go to bed on an empty stomach".

11 Postscript

In the following we have sought to summarise the conclusions of the report in a mnemonic based on the principle which we regard as pivotal, that is, the need for dialogue:

- D Debate** - Make room and time for public polycentric debate within the forums between scientists, between decision-makers and between lay people. Make sure that there is room for disagreement and promote "cooperation despite disagreement".
- I Interdisciplinarity** - Academics from different disciplines must exchange experience and work towards the creation of a mutual understanding and interpretation of and implementation of ethical principles in concepts involving biotechnology.
- A Agora marketplace** - governance and decision-makers should facilitate the creation of an agora, where stakeholders can meet and exchange views with each other and the public. In ancient Greece the public administration, the court, the philosophers and the traders met here to govern, exchange views and do business. In a time where science and the application of science is multinational and will have impact on future generations, the creation of agorae should be local, national and international alike.
- L Learning** - Children, young persons and laymen as such should be trained in decision-making with regard to ethical issues, and researchers should be educated in ethical issues concerning their field of research.
- O Operationalise** - Ensure the operationalisation of ethical principles in politics, regulation and debate.
- G Gradualism** - If we are to go forward then we should do so step by step. The principle of gradualism should be considered each time we have to make decisions that may be irreversible or may have impact on the environment and future generations.
- U Update** - Ethics "just in time" - timing - renew and update the deliberations and decisions. Choose the right time for the debate of a special issue, not too early and not too late.
- E Evolution** - of ethical principles and their specific application to new areas.

Curriculum Vitae

Master of Laws MS BERIT ANDERSEN FABER

Born 1956, LLM from the University of Copenhagen in 1985, multidisciplinary courses in the Department of Education, Philosophy and Rhetoric 1982-83 in philosophy of science and argumentation theory.

Head of secretariat in the Danish Council of Ethics in 2002, acting head of secretariat 1997-2000. Has previously worked as: special consultant at the Centre for Bioethics and Risk Assessment, the Royal Veterinary and Agricultural University, consultant for the Management Secretariat at the University of Copenhagen - committee work on university faculty networking in connection with biotechnology, chief consultant for the Danish Central Scientific Ethical Committee and administrative officer in the Danish Ministry of Health.

Rector, Professor, Doctor of Law

LINDA NIELSEN

Born 1952, LLM from the University of Copenhagen 1976. After a period as civil servant Linda Nielsen joined the Faculty of Law at the University of Copenhagen in 1979. She completed her doctoral thesis in 1993, and was appointed professor of Law in 1996. Rector of the University of Copenhagen since February 2002. Linda Nielsen has been chairman and member of a great number of Councils, Law Reform Commissions etc. nationally and internationally: From 1997 to 2000 chairman of the Danish Council of Ethics; former chairman of the Nordic Committee of Bioethics, and presently chairman of an expert group on biotechnology and ethics, serving as advisory body to a task force set down by the Danish Government. Linda Nielsen is a member of EGE, (European Group on Ethics in Science and New Technologies), advisory board to the European Commission and is serving as an expert in the evaluation of EU-Biotech projects (Ethical, Legal and Social aspects). Additionally, she was from 1998 to 2001 member of The Council of Europe's standing bureau on ethics committees (COMETH).

She is the author of numerous articles, papers and international presentations on comparative bio-law, including the relation between bio-law and bio-ethics in different legal systems.

[illegible]

[illegible]

